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Original Communications

THE MANAGEMENT OF CARCINOMA OF THE CORPUS*

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THE treatment of cancer of the endometrium is, by general consensus in this country, surgical. The preliminary application of radiation has been made successfully by some and less successfully by others, and is the subject of continued discussion. This report of the results of treatment of cancer of the corpus in the years 1938-1948, inclusive, in the Sloane Hospital for Women, covers a decade when the standard form of therapy was the preoperative installation of intracavitary radium followed by hysterectomy six to eight weeks later.

The report of this experience we believe still to be of value despite the current emphasis on experiment and a priori thinking. It is important to the therapist who is striving for improvement in results. It is more important to the layman to know that, when localized to the uterus, about 90 per cent of cases of cancer of the corpus can be cured by either method. Such knowledge will counteract the prevailing belief that all cancer is incurable and will stimulate the layman to seek early diagnosis. To almost the same degree the general physician should also be informed. Unless he is certain that early diagnosis will lead to cure, he will have no great enthusiasm for seeking out early cancer.

Our principal purpose is to study the results of the treatment of cancer of the corpus, and especially the role of radiation; second, to present some observations having to do with the background of cancer; and, third, to study some factors which seem to influence the prognosis.

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NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

In the background of cancer there was, during the ten years covering this study, a marked increase in the incidence of all uterine cancer in this hospital but a more striking elevation of the proportion of corpus cancer in relation to cancer of the cervix. Figs. 1 and 2 are graphs showing the incidence of uterine cancer from 1917-1937, inclusive, and 1938-1947, inclusive. In the first (twenty-year) period there were 143 cases of corpus cancer and 433 cases of cancer of the cervix. In the second (ten-year) period there were 216 cases of cancer of the corpus and 370 cases of cancer of the cervix. The 35 cases treated in 1948 are not included.

More striking is the change in the ratio of corpus to cervix cancer. In the earlier period it was about one of corpus to three of cervix; in the later period, about two of corpus to three of cervix.

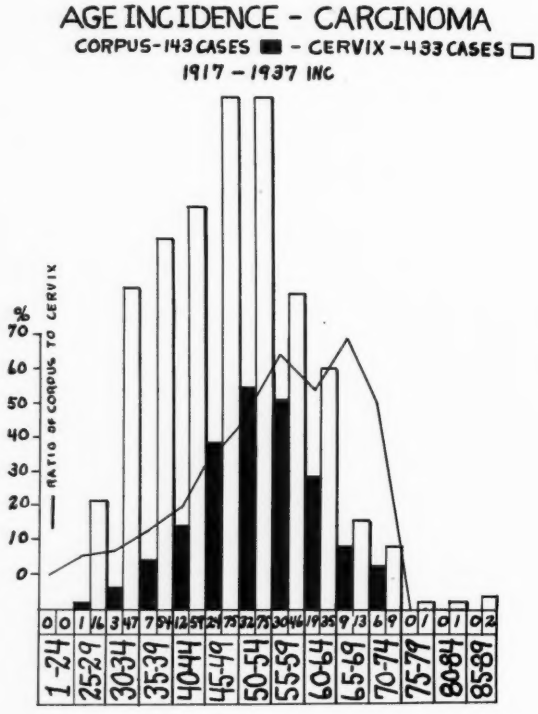


Fig. 1.—Graph showing admissions, 1917 to 1937 inclusive, for cancer of the cervix and cancer of the corpus in different age groups. The incidence of the corpus cases always remains lower than that of the cervix cases.

This change may have depended in slight degree on a change in the type of case being referred to this hospital or possibly to a greater interest in cancer on the part of the Staff. It is difficult to see any such influence. More striking is the change in the population in the different decades of life. In the graph this shows in the age levels at which there was an increase. In the old series there was a greater number of cervix cases at all ages. In the recent series the incidence of corpus cases begins to exceed that of the cervix at age 50 and remains high until the end of the graph.

Other factors remain about the same as in our previous experience.[1]

The marital status was: 210, or 85 per cent, married; 37, or 15 per cent, unmarried. In 4 cases it was not recorded.

Parity remains low. Of 218 women, 146, or 67 per cent, had borne children. Seventy-two, or 33 per cent, were nulliparous. In 33 cases parity was not recorded.

The economic status also remains unchanged. One hundred fifty-four, or 59 per cent, were private patients while 97, or 41 per cent, were in the public wards. This basis for estimating the economic status will probably have to be altered somewhat because of the role played by prepaid insurance. Some patients, who in the past would have entered the ward, now become semiprivate patients.

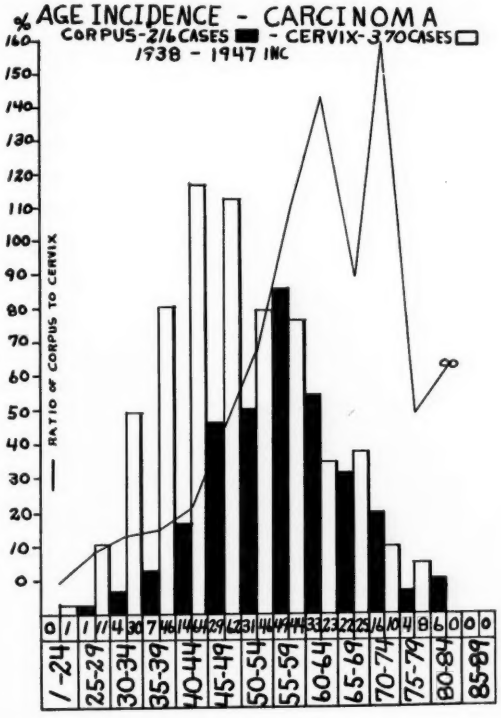


Fig. 2.—Graph showing admissions, 1938 to 1947, inclusive, for cancers of the uterus to show the great increase in the proportion of corpus cancers after age 50. Compare with Fig. 1.

Weight remains high, the average being 163.8 pounds.

There was one granulosa-cell tumor. Six patients had taken more or less continuously some form of estrogen. These points are the subject of another study.

Fourteen patients had had a radiotherapeutic menopause. These constitute 5.5 per cent of the whole series. Eleven of these women had been treated by x-ray; 2 by radium. In one case the agent was unknown. Radium certainly was not guilty of being a carcinogenic agent.

The interval between the application of radiation and the onset of cancer was two to twenty-four years; in one case 2 years; in one case 5 years; in 5 cases 8 to 9 years; in 3 cases 10 to 14 years; and in 4 cases 15 to 24 years.

Twelve patients were in the private pavilion, 2 in the public ward.

Following treatment for the cancer, 8 are well; 3 died of cancer; and 3 were not followed.

Preventive Treatment

Prophylactic hysterectomy and abstinence from estrogens seem to be the only methods available for preventing the occurrence of carcinoma of the corpus.

When uterine bleeding becomes severe enough to require destructive treatment, the problem resolves itself into a choice between hysterectomy and a radiotherapeutic menopause. At the time when the 14 patients here reported received their radiation menopause, there was much in favor of it. Had all the women who were treated similarly by radiation been treated by hysterectomy, there would have been a much greater loss from postoperative death than occurred in the cases of the 3 women who died of subsequent cancer.

Nowadays the risk of death by operation has been so reduced that hysterectomy for these benign cases should be the rule, but there must be almost no operative risk. In a technically difficult case, the surgeon must be familiar enough with the results to be expected from radiation to have the courage occasionally to close the abdomen.

Active Treatment

Of 251 patients with diagnoses of carcinoma of the corpus, 5 received no therapy. Of these, 3 had only a diagnostic curettage, twice in terminal cases and once in a patient who went elsewhere for therapy. In 2 cases an exploratory laparotomy revealed such widespread carcinomatosis that no therapy was undertaken.

Of the 246 remaining patients, 57 were treated by intracavitary radium with or without subsequent x-ray; 62 by some type of operation with and without x-ray; and 127 by preoperative radium followed 6 to 8 weeks later by hysterectomy. The crude results following the three methods of treatment are given in Table I, first by considering all patients not followed and those who died of intercurrent disease as dead of cancer, and, second, by considering only those whose fate is known.

TABLE I. CRUDE RESULTS OF TREATMENT OF CARCINOMA OF THE CORPUS

METHOD	TOTAL CASES	CASES NOT FOLLOWED	CASES FOLLOWED	WELL		LATER CARCINOMAS
				NUMBER	%	
Radiation	57	—	—	13	22.8	4
	57	18	39	13	33.3	
Operation	62	—	—	34	54.9	1
	62	11	51	34	66.6	
Radiation and operation	127	—	—	87	68.5	3
	127	22	105	87	82.8	

The former method was devised because of dishonesty in reporting results of cancer therapy. It may be good for the moral fiber of the reporter but does not make for accuracy. From a fairly long experience in the details of follow-up work, I can say with considerable assurance that it is much more difficult to trace a woman who is alive than it is to get information of her death, so that if a patient is lost to follow-up, there is greater likelihood that she is alive than that she is dead. Therefore, the use of cases which have been actually followed gives a figure which is more valid and is, if anything, on the conservative side.

From these figures it appears that 33.3 per cent of cases are cured (for 5 years) by radium; 66.6 per cent by operation; and 82.8 per cent by preoperative radium followed by hysterectomy. We shall now try to break down the crude results in order to correct as far as possible statistical errors due to selection of cases.

Treatment by Intracavitary Radium.—

Table II gives the crude results of treatment by intracavitary radium in doses called adequate when above 4,000 mg. hr. and inadequate when below 4,000 mg. hr., with and without supplementary x-ray. In nearly all cases radium was inserted at the time of the curettage. In 3 patients the x-ray preceded the radium and in 3 followed an exploratory operation at which the extent of the lesion in the parametrium made hysterectomy inadvisable.

Of the 39 patients who had been followed, 13 survived five years (33.3 per cent). Four of these had recurrences later; one of them after ten years. She had lost 100 pounds and had become "operable" and is well three years after the operation.

TABLE II. RADIUM TREATMENT OF CANCER OF THE CORPUS

METHOD	TOTAL CASES	N.F.	D.I.	D.PO	AC	DC	WELL NO.	WELL %	LATER CARCINOMA
D.C., Ra. adequate	31	10	3	0	1	12	5		3
D.C., Ra. inadequate	8	2	0	1	0	4	1		
D.C., Ra. adequate + x-ray	10	1	1	0	2	4	2		
D.C., Ra. inadequate + x-ray	3	1	0	0	0	1	1		
D.C., x-ray + Ra.	2	0	0	0	0	0	2		1
D.C., Expl. lap., Ra., x-ray	3	0	0	0	0	1	2		
Total	57	14	4	1	3	22	13	22.8	4
	18								
Cases followed	39						13	33.3	

Abbreviations.—The following abbreviations will be used in the tables:
BSO, bilateral salpingo-oophorectomy.
C.H., complete abdominal hysterectomy.
D.C., dilatation and curettage.
Expl. lap., exploratory laparotomy.
Ra., radium.
SVH, supravaginal hysterectomy.
Vag. hyst., vaginal hysterectomy.
N.F., not followed.
D.I., died of intercurrent disease.
D.PO, postoperative death.
AC, alive with cancer.
DC, died of cancer.
Well, clinically free of symptoms or physical signs of cancer.
Later Ca., cancer which reappeared later than 5 years after operation.

Table III gives the results according to the extent of the disease. Twenty cases were classed as inoperable. Of these, 3 patients survived. In 2 the parametrial extension was discovered at operation and was treated by heavy radiation by tandem in one case and by interstitial radiation in the other.

Twenty-six patients were "technically" operable, i.e., had some general condition or obesity which contraindicated operation. Of the 18 patients followed, 8 survived.

Eleven patients were "operable" although treated solely by radiation. In 2 cases the reason is not given; in one, the patient chose this form of treatment. In 8 radium was inserted as a preliminary to a proposed operation which was refused by the patient. Six of these were not followed because of the patients' refusal to return or to cooperate.

TABLE III. RADIUM RESULTS AND EXTENT OF DISEASE

METHOD	OPERABLE	TECHNICALLY OPERABLE	CERVIX	VAGINA	PARAMETRIUM	ADNEXA	MULTIPLE	RECURRENT IN STUMP	RECURRENT AFTER Ra.
D.C., Ra. adequate	7	16	1	2	1	0	2	1	1
D.C., Ra. inadequate	3	3	–	–	–	–	–	1	1
D.C., Ra. adequate x-ray	1	5	2	–	2	–	–	–	–
D.C., Ra. inadequate x-ray	–	1	–	1	–	1	–	–	–
D.C., x-ray, Ra.	–	1	–	–	1	–	–	–	–
D.C., Expl. lap., Ra., x-ray	–	–	–	–	3	–	–	–	–
Total	11	26	3	3	7	1	2	2	2
N.F.	6	3	1	–	–	1	1	2	–
D.I.	–	4	–	–	–	–	–	–	–
D.PO	–	1	–	–	–	–	–	–	–
AC	1	1	–	–	–	–	–	–	1
DC	2	9	2	3	4	–	1	–	1
Well	2	8	–	–	3	–	–	–	–
	11	26	3	3	7	1	2	2	2

The techniques of administration of intracavitary radium in this series, both in the cases treated by radiation alone and those that had a later operation, were much less efficient than is the technique used today. In 34 cases the radium was applied in a tandem which gives an ineffective distribution of radiation. If it lies in the midline, 4,000 mg. hr. delivers to each horn of the uterus an ineffective dose of radiation.[2] If it falls to one side, it will deliver in a normal-sized uterus a sublethal gamma roentgen dose to an area of about 2 sq. cm. Fig. 3 shows a uterus thought to be carcinomatous but actually the site of adenomatous hyperplasia, removed three weeks after the insertion of radium. The narrow limits of the radium effect as indicated by the ulcer in the endometrium are obvious.

In 150 patients radium was applied in a hysterostat formed by three spring wires which spread the radium in the form of a trident, Fig. 4. The principle was good but the accomplishment less than planned. In many cases the wires were crowded together by the narrowness of the lower uterine canal so as to form a widened tandem. While the distribution of radiation was an improvement over that of the tandem, it was inferior to that from the packing technique now used.

Treatment by X-ray.—

The use of x-ray has been casual and inconstant. The reason for this lies in the fact that during this period cancer of the corpus was regarded primarily

as a surgical disease and radium was considered to be only an adjuvant. At the same time the radiologists were under the influence of Regaud,[3] who had demonstrated in the bull's testes the resistance of adenomatous tissue to radiation and made from this observation the generalization that all adenomatous neoplasms were resistant.

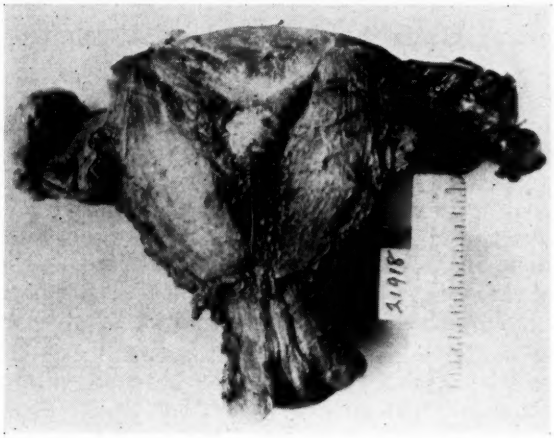


Fig. 3.—To show the limited effects of radium on the endometrium by a tandem applicator.

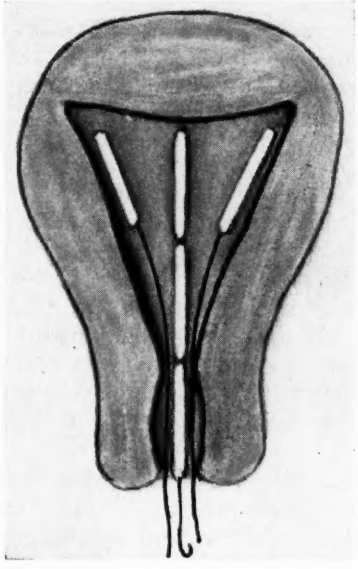


Fig. 4.—Trident-shaped arrangement of radium sources used in the majority of the cases.

I am convinced that these attitudes are not justified by subsequent observations and that x-ray, particularly in the higher voltages, should be an integral part of the treatment of any cancer of the endometrium not clearly limited to the corpus.

This conclusion is supported by the experience of Miller and Lampe,[4] who achieved a five-year survival of 88 per cent in cases treated by preoperative external x-ray; the clear-cut correlation between improvement in clinical re-

sults and improvement in x-ray therapy observed by Leucutia,[5] especially with high voltage; the experience of Masson,[6] who gave x-ray only in those cases in which the cancer was anaplastic or widespread, and obtained a higher cure rate (67 per cent) in the cases so treated than he did by operation alone in the "good" cases (66 per cent); also the observation by Stowe[7] of a correlation between heavy x-ray therapy and absence of residual cancer in specimens removed after radiation.

The experience of Wintz[8] has usually been discounted but should be reviewed.

Our own experience points in the same direction. Among the cases treated solely by radiation, 24 patients were treated by radium alone and 6 survived; whereas of 15 who received supplementary external x-ray therapy, 7 survived. These numbers are statistically invalid but are suggestive. In individual cases where intensive x-ray was given, there was a striking reduction in the size of large uteri. Masses the size of a three months pregnant uterus have shrunk to normal dimensions in a few months. One of these was so moth-eaten that the surgeon dared not insert radium. In another patient an implant in the abdominal wound disappeared completely (followed for 15 years).

Although this evidence is scattered, it seems to us to show that x-ray therapy, especially with higher voltages, has been an important factor in the treatment of carcinoma of the corpus.

The manner in which the radium is applied is of equal importance. Nearly all of the applications here were of low intensity, 50 mg. for 80 hours. All of the treatments were given in single applications which, I am sure, reduces the effectiveness of the treatment. The administration of the radium in two or more doses given 3 to 5 weeks apart should elevate our five-year results in those cases treated by radiation alone. Whether this would add to the results as a preliminary to hysterectomy it is difficult to say. Probably the best therapy would be to insert radium, give a course of x-ray therapy, and then operate, if the carcinoma is at all locally extensive.

Treatment by Operation.—

Table IV presents the results of operative treatment of corpus cancer. Table IV, *A* gives the cases in which operation was complete. Table IV, *B* gives the cases in which the adnexa or the cervix were not removed. Table IV, *C* gives the crude results of all operations. Of 62 patients operated upon, 34 survived (54.9 per cent). If only those are considered who were followed for five years or until they died of cancer, there were 51 patients, giving a survival rate of 66.6 per cent which will be used in comparisons to be made with the other method. The use of external x-ray was unsystematic. The cases are not specified in the tables.

Contemplation of Table IV, *A* and *B*, makes it apparent, in discussing the operative treatment of carcinoma of the corpus, that we are not dealing with a single operative procedure which could be compared with some other form of therapy but with a number of procedures, some of which bring about a thorough removal of the uterus and adnexa while others are grossly incomplete.

Second, the table reveals the apparent paradox that the patients incompletely operated upon have a better survival rate than those whose operation has been thorough. This apparent superiority of the incomplete operation is explained by the large number of cases in which the tumor was very small. Seven of these were so small as to have been overlooked during operations for other lesions. These cases will appear again when the results of operation are compared with those following the combined method.

TABLE IV. RESULTS OF OPERATION WITHOUT PREVIOUS RADIUM

METHOD	TOTAL CASES	N.F.	D.I.	D.PO	AC	DC	WELL NO.	WELL %	LATER CA.
A. Complete Operation.—									
C.H., BSO	43	8	–	–	1	11	23		1
Radical hyst.	1	–	–	–	–	1	–		–
Total	44	8			1	12	23	52.3	1
	8								
Cases followed	36						23	64.0	
B. Incomplete Operation.—									
C.H.	3	–	–	–	–	–	3		–
Vag. hyst.	3	–	–	–	–	–	3		–
SVH	5	1	–	–	–	3	1		–
SVH, BSO	7	2	–	–	–	1	4		–
Total	18	3				4	11	61.0	
	3								
Cases followed	15						11	73.0	
C. Grand Total									
	62	11			1	16	34	54.9	
	11								
Cases followed	51						34	66.6	

TABLE V. OPERATIVE RESULTS RELATED TO EXTENT OF DISEASE

METHOD	CURED BY D.C.	ADENOMA MALIGNUM	HYPERPLASIA	POLYP	ENDOMETRIUM	SUPERFICIAL MUSCLE	DEEP MUSCLE	CERVIX / VAGINA / PARAMETRIUM	ADNEXA MICRO.	ADNEXA GROSS	LYMPH NODES	MULTIPLE	RECURRENT IN STUMP	RECURRENT AFTER Ra.
C.H., BSO	1	2	7	1	2	5	4		11	5	–	5	–	–
Radical hyst.	–	–	–	–	–	–	–		–	–	–	–	–	1
C.H.	–	–	2	–	–	1	–		–	–	–	–	–	–
Vag. hyst.	–	–	–	–	–	3	–		–	–	–	–	–	–
SVH	1	–	–	–	–	–	1		–	2	–	1	–	–
SVH, BSO	–	–	–	–	–	1	1		–	3		2	–	–
Total cases	2	2	9	1	2	10	6		11	10		8		1
RESULTS														
N.F.	–	1	3	–	–	2	1		2	1	–	1	–	–
D.I.														
D.PO														
AC	–	–	–	–	–	–	–		1	–	–	–	–	–
DC							1		2	5	–	7	–	1
Well	2	1	6	1	2	8	4		6	4	–	–	–	–
	EARLY				LOCAL			EXTENSION	METASTASIS					
Total followed	10				15				9	9	7		1	
Total well	10				14				6	4	0		0	
Per cent	100.0				93.3				66.6	44.4				

From another standpoint these cases may have a significant bearing on the question of lymph node metastases and extended operations. The high cure rate among patients treated by incomplete surgery suggests that carcinoma of the corpus remains localized a long time and that metastases are late and may be perhaps infrequent, the result of a specific lethal quality which permits the metastases to survive in the new environment rather than being a mere transportation of cells all having the same biological potential.

Another table prepared to show whether a diagnostic curettage added to the effectiveness of an operation showed that, where the dilatation and curettage was performed, there was a 71.4 per cent five-year survival, whereas, when it was omitted, there was a survival of only 56.2 per cent.

The correlation between the extent of the disease and survival is given in Table V. For this purpose none of the suggested classifications was satisfactory. We therefore classified the cases as "very early," "localized" to the corpus; locally "extended" to the cervix, parametria, or vagina, and "metastatic."

The group called "early" consists of (1) cases in which the cancer was apparently completely removed by the curette, (2) cases of adenoma malignum, (3) cases in which true carcinoma was mixed with adenomatous hyperplasia, and (4) cases in which there was carcinomatous change in a polyp.

TABLE VI. RESULTS OF PREOPERATIVE RADIUM AND OPERATION

METHOD	TOTAL CASES	N.F.	D.I.	D.PO	AC	DC	WELL NO.	WELL %	LATER Ca.
D.C., Ra. adequate, C.H., BSO	60	6	–	1	1	8	44		2
D.C., Ra. inadequate, C.H., BSO	62	12	3	–	–	6	41		2
D.C., x-ray, C.H., BSO	1	–	–	–	–	–	1		
D.C., Ra. adequate, SVH, BSO	3	1	–	–	–	1	1		
D.C., Ra. inadequate, SVH, BSO	1	–	–	1	–	–	–		
	127	19	3	2	1	15	87	68.5	4
	22								
Cases followed	105						87	82.8	
Completely operated upon	123						86	69.7	
	21								
Cases followed	102						86	84.3	

The term carcinoma in situ has been suggested for these lesions which are limited to the endometrium. The cases here listed were all cancers. Those with wild hyperplasia but no break through ("nicht Karzinom aber besser heraus") have been excluded. It would be a mistake to treat all of these lesions as simple superficial noninvasive cancers. Two cases with microscopic ovarian metastases had in the uterus this picture of adenomatous hyperplasia mingled with carcinoma and had it not been for the metastasis, would have been called "early."

"Local" lesions are those frank adenocarcinomas which are localized to the corpus.

"Extension" implies that the lesion has spread by local extension to the cervix, vagina, or parametrium.

"Metastasis" includes cases with microscopic and gross metastasis to the ovary and tube, isolated metastasis to the regional lymph nodes, and "multiple" metastases with involvement of several structures (peritoneum, omentum, intestine, bladder, aortic nodes). There was no case described in which involvement of the regional nodes existed without extension to other structures.

The results will be discussed in detail when they are compared with the results following the combined method.

Treatment by Preoperative Radium Followed by Hysterectomy.—

These cases are more easily arranged for study. The diagnosis was known in all cases and the operation was complete in all but 4 in which, because of extent of disease or technical difficulty, it was curtailed. Of the 105 patients who were followed, 87 survived (82.8 per cent). Of the 102 patients completely operated upon, 86 survived (84.3 per cent) (Table VI).

The results according to the extent of the disease (Table VII) were less easily tabulated because of difficulty in establishing the extent of the disease at the time the radium was administered. This will be discussed in more detail when the two methods are compared.

TABLE VII. RESULTS RELATED TO EXTENSION OF DISEASE

METHOD	CURED BY D.C.	ADENOMA MALIGNUM	HYPERPLASIA + Ca.	POLYP	ENDOMETRIUM	SUPERFICIAL MUSCLE	DEEP MUSCLE	CERVIX	VAGINA	PARAMETRIUM	ADNEXA MICRO.	ADNEXA GROSS	LYMPH NODES	MULTIPLE
D.C., Ra. adequate, C.H., BSO	2	–	–	–	2	22	24	3	–	–	5	2	–	1
D.C., Ra. inadequate, C.H., BSO	1	1	2	–	6	18	19	1	1	–	12	–	–	–
D.C., x-ray, C.H., BSO	–	–	–	–	–	–	–	1	–	–	–	–	–	–
D.C., Ra. adequate, SVH, BSO	–	–	–	–	–	1	1	–	–	–	–	–	–	1
D.C., Ra. inadequate, SVH, BSO	–	–	–	–	–	–	–	–	–	1	–	–	–	–
	3	1	2	–	8	41	44	5	1	1	17	2	–	2
N.F.	2	–	1	–	2	7	5	–	–	–	1	–	–	1
D.I.	–	–	–	–	–	1	2	–	–	–	–	–	–	–
D.PO	–	–	–	–	–	–	1	–	–	1	–	–	–	–
AC	–	–	–	–	–	–	1	–	–	–	–	–	–	–
DC	–	–	–	–	–	1	7	1	1	–	3	1	–	1
Well	1	1	1	–	6	32	28	4	–	–	13	1	–	–
	EARLY				LOCAL			EXTENSION			METASTASIS			
Total followed	3				76			7			16	2		1
Total well	3				66			4			13	1		0
Per cent	100.0				86.8			57.1			73.5			

Comparison of Results of Treatment by Operation Alone and by Intracavitary Radium Followed by Operation

Table VIII is a combination of the totals of Tables V and VII. It shows a crude five-year salvage of 66.6 per cent in cases treated by operation alone and of 82.8 per cent when the operation was preceded by intracavitary radium. We believe that these figures are fairly reliable. Their validity depends on whether the cases in which the two methods were used were comparable.

TABLE VIII. COMPARISON OF RESULTS OF OPERATION WITH AND WITHOUT PREOPERATIVE RADIUM

	EXTENT OF DISEASE															TOTAL
	CURED BY D.C.	ADENOMA MALIGNUM	HYPERPLASIA + Ca.	POLYP.	ENDOMETRIUM	SUPERFICIAL MUSCLE	DEEP MUSCLE	CERVIX	VAGINA	PARAMETRIUM	ADNEXA MICRO.	ADNEXA GROSS	LYMPH NODES	MULTIPLE	
Radium Followed by Operation.—															
No. of cases	1	1	1	0	6	33	37	5	1	1	16	2	–	1	
No. well	1	1	1	0	6	32	28	4	0	0	13	1	–	0	
	EARLY				LOCAL			EXTENSION			METASTASIS				
No. of cases	3				76			7			19				105
No. well	3				66			4			14				87
%	100.0				86.8			57.1			73.7				82.8
Operation Alone.—															
No. of cases	2	1	6	1	2	8	5				9	9	–	8	
No. well	2	1	6	1	2	8	4				6	4	–	0	
	EARLY				LOCAL						METASTASIS				
No. of cases	10				15						26				51
No. well	10				14						10				34
%	100.0				93.3						38.4				66.6

Very quickly it becomes apparent that they are not. The cases treated by operation alone were concentrated at the two extremes. Ten out of 51 (20 per cent) of the cases were "very early" and almost automatically curable and 8 out of 51 (15.7 per cent) had "multiple" metastases and were hopeless. There were also 9 of the 51 cases (17.4 per cent) with gross involvement of the adnexa. Only 15 of the 51 (21 per cent) were frank cancers localized to the corpus. There were no cases in which the tumor had extended locally.

On the other hand, the cases treated by preoperative radium were concentrated under the heading "localized," i.e., frank cancer localized to the corpus (76 in 105, or 72.3 per cent). And there were 7 cases in which the cancer had extended locally. There were only 3 out of 105 (3 per cent) "very early cases," 1 in 105 (1 per cent) completely hopeless, and 1 in 105 (1 per cent) with gross metastasis in the ovary.

The proportion of microscopic metastases to the adnexa was fairly even, 16 of 105 (15.3 per cent) in the cases treated by the combined method and 9 of 57 (15.8 per cent) treated by operation alone.

This difference of distribution is explained by the fact that, in the decade being studied, preoperative radium followed by hysterectomy a few weeks later was the standard treatment. If the operator encountered a massive cancer limited to the uterus or locally extended, he would apply radium and operate later.

If, on the other hand, the presence of the carcinoma was overlooked, he would operate for the presenting condition. The carcinoma would be picked up in the laboratory. This happened in the presence of a coincident primary

ovarian cyst (4 cases); myomatous uterus (10 cases). At other times an ovary enlarged by metastasis would be misdiagnosed as a primary ovarian tumor (3 cases). Operations were performed for menopausal bleeding thought to be benign. Three vaginal hysterectomies were performed as part of plastic procedures. As seen in Table IV these mistaken diagnoses yielded a variety of operations in which, because of the smallness of the carcinoma, incomplete operations gave better results than those which were thorough.

At the other extreme were cases obviously so extensive that the local effect of the radium would be ineffective.

Results.—

Breaking down the results according to the extent of the disease we find that by either method of treatment all of the "early" cases were cured. In the cases in which the lesion was apparently confined to the corpus, the proportion of cures by either method was about equal.

Similarly the results in cases with adnexal metastases were approximately the same in the two groups. The number of five-year cures is surprisingly high and aroused the doubts of some to whom the figures were shown. The slides were again reviewed and four cases were excluded: one which might be called endometriosis and three in which the deposits of cancer cells were so superficial as to suggest the possibility of an artifact, the deposition of tissue on the surface of the ovary during the preparation of the blocks. Had these been included, there would have been 20 cases treated by the combined method with a survival of 17, or 80 per cent.

Finally, by neither method were any widespread lesions cured.

Column by column there seems to be no great difference in the percentage of cures obtained by either method. How, then, can we account for the 82.8 per cent salvage following the combined technique as compared with the 66.6 per cent of operation alone? The answer lies in the large number of cases treated by the combined method in which the lesions were localized to the corpus, 76 of the 105 cases so treated being in this group. It will be necessary, therefore, to see if the cases limited to the corpus and treated by one method are comparable to those treated by the other.

In the cases treated by surgery, this is fairly easy. The lesions in the uterine wall were little altered by the curettage and the histologic picture was of course unmodified by any treatment.

The cases treated by preoperative radium, on the other hand, were not so readily defined. The original observations of size of uterus, depth of uterus, consistence of uterus were not uniform and were hampered by the obesity of the patients (average weight 164 pounds).

The specimens, when removed, were found to be strikingly altered by the radium. The uteri were all reduced in size. In some a uterus described as being the size of a three months' pregnancy had been reduced to the size of a normal or less than normal uterus. Large fungating masses had disappeared, leaving only a whitish plaque of radium eschar. The identification of the stage of the disease, therefore, was the result of the observation at the time

of the curettage and that made when the uterus was removed. The histologic picture was taken from the original specimen and changes in the operative specimen noted.

With these limitations in mind, a comparison of the localized lesions in the two groups will be made. Of the 15 cases treated by operation, there were 2 massive cancers occupying most of the uterine cavity. The other lesions were all small. In 6 the presence of the cancer was unsuspected at operation and was discovered in the laboratory. Of these, 2 were operated upon for ovarian cyst by supracervical hysterectomy and bilateral salpingo-oophorectomy; 3 had vaginal hysterectomy as part of a plastic procedure on the pelvic outlet. The adnexa were untouched. In one case the curettings were considered grossly benign and an immediate hysterectomy was performed with conservation of the adnexa. In 9 cases in which the diagnosis was known, there were 4 small polypoid lesions, 4 fungating lesions less than 2 cm. in diameter, and one in which no lesion could be found grossly after the curettage.

The 76 cases treated by preoperative radium were divided into those in which the uterus was not enlarged (29 cases), those in which the uterus had reached the size of a two months' pregnancy (24 cases), and those in which the uterus had reached the size of a three months' pregnancy (12 cases). In 4 of the latter, fibroids caused part of the enlargement. In 11 the original extent of the lesion was not clear. They will be grouped with the cases in which the uterus was not enlarged.

As we attempt to compare the two types of therapy, we run into a statistical dead end. While we can compare the 15 cases operated upon (one death) with the 40 cases treated by the combined method (4 deaths), we have no cases operated upon to compare with the 24 cases with moderately enlarged uteri (4 deaths) and the 12 cases with greatly enlarged uteri (2 deaths) treated by the combined method.

Comparison must be made with other reports in which the five-year results on cases classified according to Healy's[9] classification as Stage II and III were in the neighborhood of 50 per cent. This is compared with 83.4 per cent in Stage II of the cases presented here and 86.7 in Stage III. In the irradiated cases there was no spilling of gross carcinoma. None of the uteri ruptured as they were being removed. The operator dealt with a firm, easily handled structure rather than one which was soft and friable.

This impression is so strong in our own minds as to form a conclusion that radiation greatly improved the results in the bulky carcinomas limited to the uterus.

The location of recurrences has been taken as a measure of the efficiency of one or the other method of treatment. Some found a greater incidence[10] of recurrences in the vaginal vault in cases treated by preoperative radiation. More reporters found a greater incidence of vaginal recurrences in cases treated by operation alone. They attribute the fewer recurrences in the vaginal scar in the radiated cases to the cauterizing of the uterus which prevented spill of cancer cells.

Our experience is limited because we do not see these patients in their terminal stages. Of 14 observed cases of recurrent carcinoma following the combined method, one recurred in the vaginal wound. Of 7 cases recurrent after operation, 2 were located in the vaginal wound, and one in the abdominal scar. Two cases of this series recurrent after operation have apparently been cured by radiation, one by intravaginal radium and one by transvaginal x-ray. The mass in the abdominal scar was cured by x-ray (15 years' observation).

The technique of applying intracavitary radium prior to hysterectomy was similar to that used when radium was the sole agent. There was only one application. In the combined treatment the interval between the radium application and the hysterectomy was usually 6 to 8 weeks. The proposal to operate immediately meets no great objection. From the radiation standpoint the action begins with the installation of the radium and will continue whether the cancer cell be free in the vaginal wound or lying outside the field of excision. With antibiotics the danger of peritonitis is lessened. If, however, there is a large friable uterus, it had better wait until the full effects of the radium have been felt. A small, firm uterus will be removed instead of one which will be large and friable and bound to spill cancer cells despite suturing of the cervix.

Hysterectomy with or without the preliminary radium was preceded by suturing the cervix. Most operators ligated the tubes. The infundibulopelvic ligament was ligated at the pelvic wall. The uterus was removed in very much the same manner as for a benign condition, by cutting close to the uterus so as to avoid the ureters and removing a short vaginal cuff or none.

There were two radical hysterectomies, one with and one without dissection of lymph nodes.

One exenteration was performed for a recurrence in the midpelvis following hysterectomy.

We can present nothing which would bear directly on the importance of metastases in the regional lymph nodes, or the desirability of performing more extended operations. Nodes were not sought for especially and, when observed, were part of a generalized process.

Indirect evidence bearing on this point is the high cure rate of 90 per cent when the lesion was limited to the uterus and the relatively high cure rate in cases in which there were microscopic metastases in the ovary, 18 in 25 (76 per cent). If metastases to the lymph nodes occurred early in the disease, one would expect a higher rate of recurrence since in none of these cases were the lymph nodes touched. Also of some significance are the results of incomplete surgery in cases of cancer localized to the uterus (Table IV, *B*). These were mainly small cancers but if they had been of a type which had a high lethal quality, i.e., a tendency to metastasize early, fewer would have survived.

From this experience we conclude that the study of the importance of the lymph nodes should continue but should be carried out only by those especially qualified and with exceptional facilities.

We believe, however, that from the evidence so far presented extensive operations should not be a matter of routine. As we see it, when involved lymph nodes have been found, the cancer mortality has not been changed much

by their removal. Second, these older women are usually not the best operative risks. Their average weight was 164 pounds. Obesity adds to the difficulty of the operation. In our Wertheim hysterectomies for cancer of the cervix, most of the important operative injuries have occurred in the obese patient. Last, the results obtained by the simple hysterectomy are so high that something very significant will have to be accomplished by the wider operation. So far this has not been apparent.

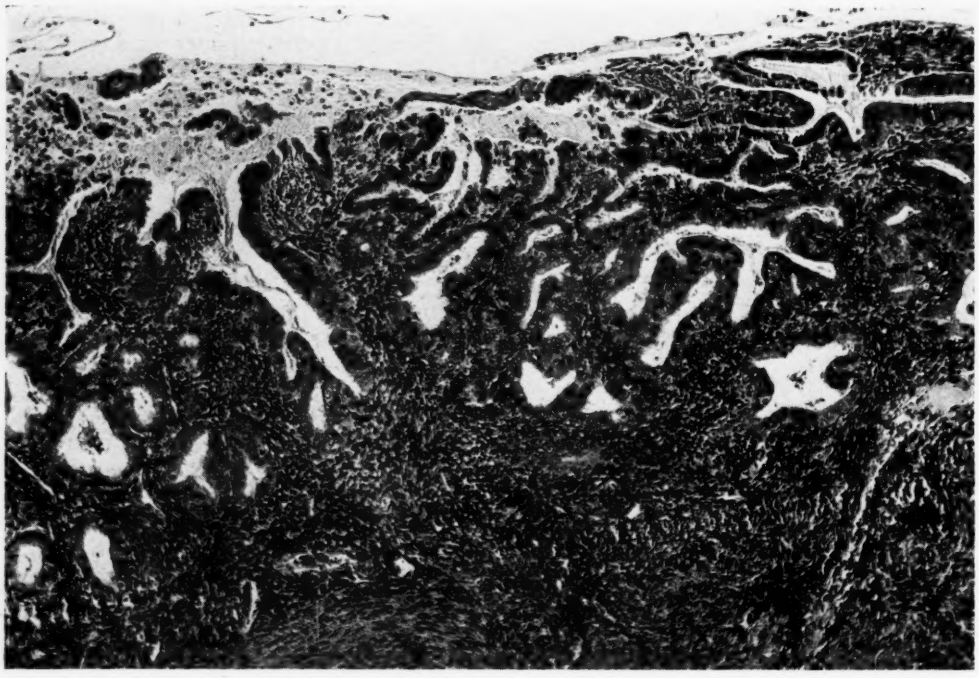


Fig. 5.—An example of Grade I adenocarcinoma of the endometrium showing no response to 4,000 mg. hr. of radium, single tandem technique. Total hysterectomy, bilateral salpingo-oophorectomy six weeks later. (Hematoxylin and eosin. ×125; reduced ¼.)

Operability.—

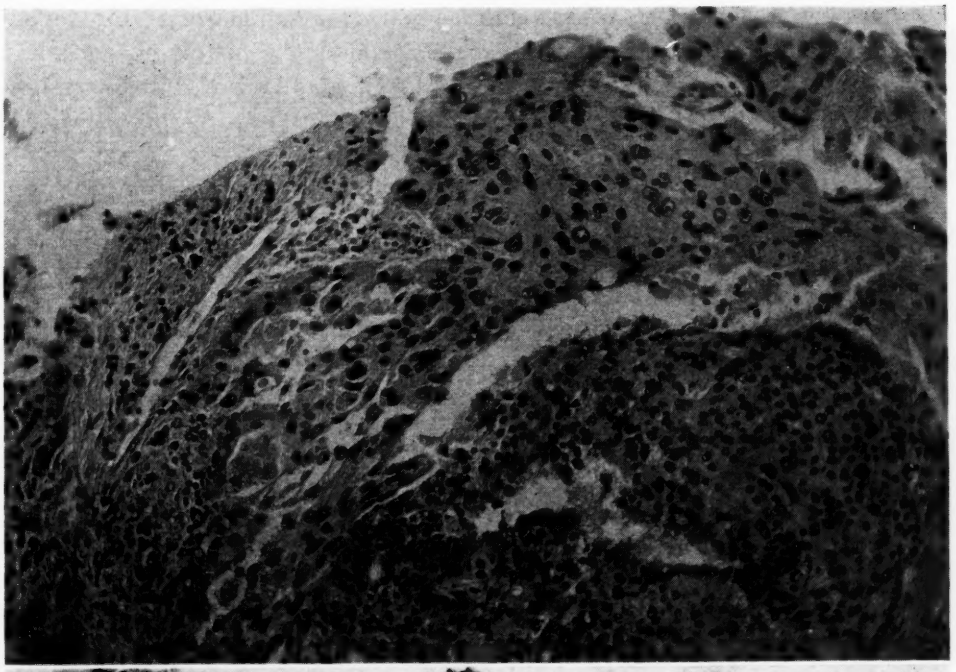
In this group of 251 cases, 205 were considered clinically operable (80 per cent); 26 were technically operable, that is operable from the technical standpoint but with some general condition which contraindicated operation, principally cardiovascular disease and obesity.

This group can be considerably reduced. Even with the equipment available in the years 1938-1948, in retrospect many of the patients classed as poor operative risks could have been operated upon. And obesity now holds fewer terrors. Through a transverse incision, a fair exposure can be made.

Injuries: These were unimportant. One patient died following exploratory operation for abdominal carcinomatosis. Two patients died of coronary thrombosis, each on the seventeenth postoperative day.

There were no vesicovaginal fistulas. There was one ureterovaginal fistula in a private patient treated by nephrectomy. The patient has been well 13 years. There was one case of severe radiodermatitis of the vulva following transvaginal x-ray for a recurrence in the vaginal vault following hysterectomy.

Fig. 6.



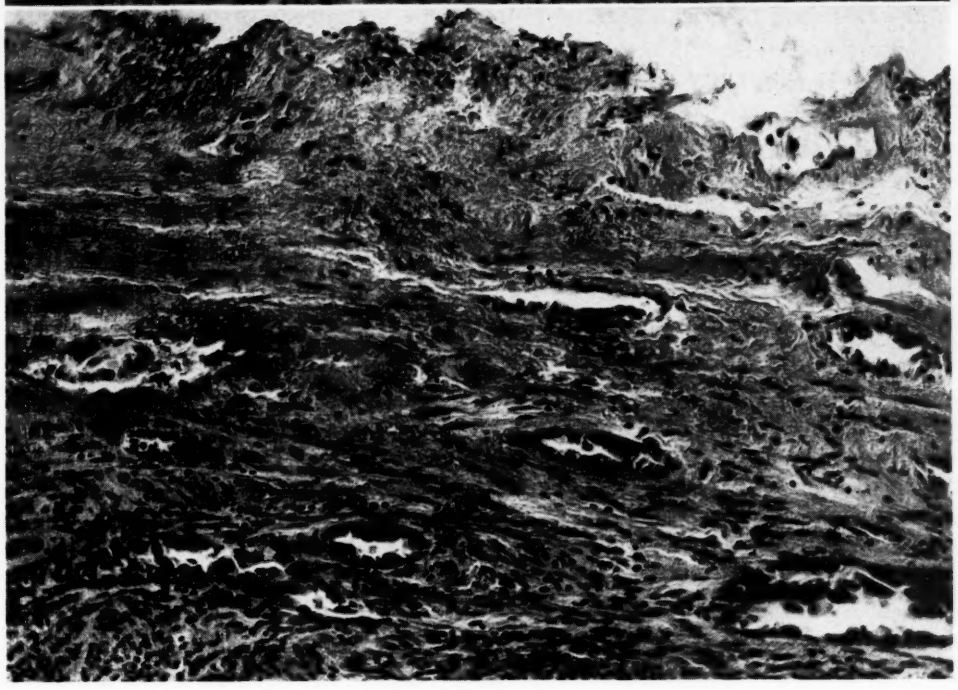


Fig. 7.

Fig. 6.—A moderate radiation response following adequate radium dosage and removal of specimen six weeks later. Many of the cells show radiation effects but are intermingled with healthy-appearing tumor cells. (Hematoxylin and eosin. ×240; reduced ¼.)

Fig. 7.—Marked radiation response showing typical radionecrotic plaque. There are no healthy tumor cells present. This tumor received adequate radium therapy six weeks prior to hysterectomy and bilateral salpingo-oophorectomy. (Hematoxylin and eosin. ×240; reduced ¼.)

Microscopic Pathology

There were 243 cases with available pathological material for review. These were studied with the purpose (a) of allotting a histological grade to each tumor, (b) of ascertaining the extent of local spread of disease, and (c) to determine the local response of the tumor to radiation in the preoperatively radiated cases.

A simplified system of three grades was employed and based on the qualitative degree of histological differentiation. Grade I tumors were well differentiated adeno-carcinomas comprising the familiar papillary and/or adenomatous pattern. Grade III comprised the totally anaplastic tumors, while Grade II tumors contained both Grade I and Grade II elements. All tumors were graded from the submitted curettings whenever possible. In this series, 74.1 per cent were Grade I, 14.3 per cent were Grade II, and 11.6 per cent were Grade III tumors.

To determine the depth of invasion the uterine wall was arbitrarily divided into three layers, endometrium, superficial myometrium, and deep myometrium. No distinction was made between direct extension and metastatic extension.

The determination of radiation response of a tumor was, of necessity, only qualitative, and limited to the tumor remaining in the endometrium and/or the myometrium. *No response* included cases with areas of healthy proliferating tumor cells either alone or adjacent to areas of malignant cells showing definite radiation changes (Fig. 5). A *moderate response* was one where a mixture of radiated and nonradiated malignant cells was present in each of every tumor-bearing area remaining (Fig. 6). A *marked response* included cases where all residual malignant cells showed characteristic radiation changes (Fig. 7).

Cases in which no residual carcinoma could be found, whether removed by curettage or necrotized by radiation as evidenced by the radiation plaques, were of necessity grouped separately. Of 123 cases, 37, or 30 per cent, had no residual tumor (Table IX).

TABLE IX. PREOPERATIVE RADIATION RESPONSE RELATED TO SURVIVAL

RADIATION RESPONSE	NO.	ALIVE 5 YEARS		DEAD	NOT FOL.
		NO.	%		
No response	15	8	53.3	5	2
Moderate response	13	11	84.6	0	2
Marked response	58	41	70.7	12	5
No Ca. seen	37	27	73.0	3	7
Total	123	87		20	16

Results.—

Table X illustrates the inverse relationship of the grade of tumor to the crude survival rate. Only 39.3 per cent of patients with Grade III or totally anaplastic tumors survived five years, while 60 per cent of patients with Grade I or well-differentiated tumors survived the same length of time.

TABLE X. SURVIVAL ACCORDING TO GRADE OF TUMOR

	GRADE I		GRADE II		GRADE III		
	NO. OF CASES	RESULT IN %	NO. CASES	RESULT IN %	NO. CASES	RESULT IN %	TOTAL CASES
Alive	108	60.0	18	51.4	11	39.3	137
Dead	32	17.8	14	40.0	12	42.9	58
N.F.	40	22.2	3	8.6	5	17.8	48
Totals	180	100.0	35	100.0	28	100.0	243

Table XI is an attempt to correlate the biological activity, that is the invasive and metastasizing potentialities of the growth, with the degree of histological differentiation. Of the Grade I tumors 62.6 per cent invaded the myometrium and 19.0 per cent metastasized to the adnexa, while 84.0 of Grade III tumors invaded the myometrium and 32.0 per cent metastasized to the adnexa.

TABLE XI. LOCAL SPREAD OF DISEASE ACCORDING TO GRADE

	INVASION OF MYOMETRIUM			METASTASES TO OVARIES AND/OR TUBES		
	TOTAL	NO. CASES	%	TOTAL	NO. CASES	%
Grade I	139	87	62.6	133	27	19.0
Grade II	24	19	79.0	23	13	49.0
Grade III	25	21	84.0	25	8	32.0

Table XII relates the crude survival rate to depth of tumor invasion. Of the patients with tumor limited to the endometrium, 85 per cent survived five years while only 41.0 per cent of those with tumor deep in the myometrium survived for the same length of time. The relatively large survival rate (78.0 per cent) in cases in which the depth of invasion could not be defined confirmed the impression gained from this study that these lesions were originally limited to the endometrium or invaded the myometrium only superficially.

There were 87 cases, or 70.0 per cent, with residual carcinoma following preoperative radium therapy (Table IX). This is in accord with the results of others in which the same technique was used.

TABLE XII. SURVIVAL RELATED TO DEPTH OF MYOMETRIAL INVASION

DEPTH OF TUMOR	TOTAL CASES	% OF TOTAL	ALIVE 5 YEARS		DEAD	N.F.
			NO.	%		
Endometrium	20	10.2	17	85.0	1	2
Superficial	73	39.3	54	74.0	10	9
Deep	56	30.1	23	41.0	22	11
No Ca. seen	38	20.4	30	78.0	2	6
Total	187		124		35	28

Conclusions

Intracavitary radium was a partially satisfactory therapy for carcinoma of the corpus. The five-year survival rate was 33.3 per cent. Four of these patients later succumbed to carcinoma.

A small percentage of cancer of the corpus (5 to 10 per cent) is very lethal, metastasizing probably before it is clinically manifest.

Cancer of the corpus in most cases remains localized in the uterus for a long time and is cured by either operation alone or intracavitary radium followed by operation. Early diagnosis is therefore desirable.

In cancers of large size involving the whole endometrium and enlarging the uterus, preoperative radium apparently gives five-year results superior to those following operation alone.

A surprisingly high percentage of five-year cures followed treatment of microscopic and gross metastatic lesions in the adnexa.

No case in which the disease had spread beyond the adnexa was cured.

The more anaplastic tumors are the more actively growing tumors and have a higher mortality than the more differentiated tumors.

The more anaplastic tumors penetrate deeper into the myometrium, and metastasize more frequently to the adnexa.

The deeper the tumor invades the myometrium, the higher is the mortality.

Cases that show no response to radiation have a higher mortality rate than the cases that do reveal a radiation response.

References

1. Corscaden, J. A., Fertig, J. W., and Gusberg, S. B.: AM. J. OBST. & GYNEC. 51: 1, 1946.
2. Corscaden, J. A.: Gynecologic Cancer, New York, 1951, Thos. Nelson & Sons.
3. Regaud, C.: Compt. rend. Soc. de biol. 86: 787, 1922.
4. Miller, N., and Lampe, I.: Personal communication.
5. Leucutia, T.: Am. J. Roentgenol. 68: 770, 1952.
6. Masson, J. C.: S. Clin. North America 27: 763, 1947.
7. Stowe, L. M.: AM. J. OBST. & GYNEC. 51: 57, 1946.
8. Wintz, H.: Strahlentherapie 69: 3, 1941.
9. Healy, W. R., and Brown, R. L.: AM. J. OBST. & GYNEC. 38: 1, 1939.
10. Javert, C. T.: AM. J. OBST. & GYNEC. 64: 780, 1952.

Discussion

DR. THOMAS C. PEIGHTAL.—At Dr. Corscaden's suggestion my discussion will deal chiefly with the incidence of pelvic lymph node metastases as demonstrated when radical surgery has been done and with the prognosis in such cases.

Dr. Corscaden has stressed the desirability of taking out of consideration, in preparing end-result statistics, that group of endometrial carcinomas which are limited to the endometrium with no or very minimal invasion of the uterine musculature. With this we are in accord.

(Further discussion was continued by the use of slides which may be summarized for printing as follows.)

Slide No. 1 shows the incidence of node metastasis in operative cases from the reports of Ingersoll, Javert, Meigs, Randall, and our own. Javert's 50 cases with 14 positive nodes (28 per cent) becomes 47 cases with 14 positive nodes (30 per cent) when 3 cases with only a superficial lesion limited to the endometrium are deducted. In our series of 9 cases 5 were considered as superficial invasion and of the 14 remaining 4 had positive nodes, or 28.5 per cent.

Slide No. 2 shows the percentage of positive nodes found at autopsy by Meigs and Henderson. One notes that, as far as pelvic nodes are concerned, there is little difference between these percentages and those found at operation in the cases when the lesion has really invaded the myometrium.

Slide No. 3 shows the relationship between the incidence of positive nodes and the depth of invasion of the uterine wall in Javert's 50 cases. Three cases limited to the endometrium had no positive nodes; in the cases of slight invasion there was one with positive node; in the cases of moderate invasion there were 3 with positive nodes; and in

the cases where the lesion was advanced almost to the serosa there were 10 with positive nodes. Thus the percentage of nodal metastasis varies with the depth of the tumor.

Does removal of the pelvic nodes improve the prognosis in carcinoma of the endometrium? If all cases were subjected to this type of radical surgery, in the approximately 70 per cent which will have no positive nodes this would be an unnecessarily radical procedure and, of course, would carry with it the usual percentage of urinary tract complications. In the 30 per cent which would have positive nodes this operation might greatly increase the salvage for the patients would most certainly die of disease if treated by radium plus average complete hysterectomy. To date, however, end results in our cases and those of Javert are not so encouraging as we had hoped for when pelvic node dissection was added to hysterectomy. In Javert's 14 cases only 4 (28 per cent) have survived four years or less. In our group of 4 with positive nodes one died of the disease in the first year, another died in the second year, while 2 are still alive at eighteen months. In a study of these specimens, cancer cells have been found not only in the lymph channels and nodes but also in the blood vessels. In the latter group early metastases outside the pelvic area might be expected and radical node dissection cannot salvage these cases. Where metastases have not extended beyond the pelvic lymphatic system removal of the nodes up to the aortic bifurcation may be expected to salvage the majority, none of whom could be saved by radium, x-ray, or less radical surgery.

It is to be emphasized that radical hysterectomy plus pelvic lymph node removal in our cases and in those done elsewhere must be thought of as an operative experiment which endeavors to add to our knowledge of the metastatic spread of carcinoma of the endometrium and, when many more cases have been done, may indicate whether or not this type of surgery will increase the percentage of five-year salvage. For the present, however, we still believe that the treatment of choice, except in these experimental groups, must remain preoperative radiation, preferably by the multiple-dose capsule method, followed by complete hysterectomy. Since, in the statistics of many clinics, salvage as high as 85 per cent has been reported in those cases with no residual disease at hysterectomy after radiation and it is not above 60 per cent where residual disease is found, one might predict that the latter figure could be improved if these cases had the additional benefit to be derived by pelvic lymph node dissection when the patient's condition would permit of such procedure. Time alone will give the answer.

DR. CARL T. JAVERT.—Dr. Corscaden has divided his material, 243 cases, in the time-honored fashion, into a group treated by preliminary radium followed by surgery and into one treated by surgery alone. His statistics show a slightly better five-year survival for those patients treated first with radium. But is not this time-honored approach subject to criticism? Most reports on other types of cancer give end results on the basis of positive and negative nodes. This has seldom been done for cancer of the endometrium.

Dr. Corscaden has asked me to comment on the occurrence of pelvic lymphatic metastases. To date some 60 of the patients cared for at the New York Hospital, have had a sampling of the pelvic nodes. This program began just five years ago, to test the generally accepted views and statements in textbooks, that pelvic lymph node metastases were rare and late manifestations of the disease. This has been disproved by the finding of positive nodes in 16, or 20 per cent, of the patients who were considered operable. Strangely enough, this study began as a project to study the lymphatic spread of endometriosis.

Twenty per cent of these patients with endometrial cancer had positive pelvic lymph node metastases. These were treated subsequently by external radiation. Nevertheless, none have survived for five years. Most of them have died within two and one-half years. Conversely, of the remaining 80 per cent with negative nodes, 85 per cent are still alive, five years or less. It appears from these meager data that the prognosis depends on the time-honored principle, viz., whether the regional nodes were positive or negative. If they are negative, nothing further need be done. If they are positive, radical lymphadenectomy should be considered, since our experience has shown no effect of x-ray on the nodes in terms of five-year survivals.

On the other hand, I am rather pessimistic regarding the curative value of radical surgery for any cancer. When I graduated from medical school in 1932 cancer was seventh as a cause of death. This situation has changed gradually in the past two decades, and now, with radical surgery in full bloom, cancer is second as a cause of death. Obviously, if present trends continue, and I speak in an era that has embraced radical surgery for cancer, I fully expect to live to a time when all deaths will be due to cancer.

I would like to emphasize the importance of lymphatic spread by referring to 10 common cancers occurring in various parts of the body. The tables may be found in an article published by me in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, vol. 64, no. 4, pages 780-806, as Tables XII, XIII, and XIV. These statistics plainly show that most of us are far behind the times, including Dr. Corscaden, unless we have knowledge of the pelvic node metastases when treating patients with endometrial cancer.

His total results in 243 patients, namely, 84 per cent with radium and 66 per cent without radium, but including operation in either group, are approximately 75 per cent, if they are combined. This signifies to me, from our experience, namely 75 per cent survival with surgery alone, when the disease was limited to the uterus, that those who survived did not have lymphatic spread; those who did are dead and gone.

When only one or two of the regional nodes have metastases, radical lymphadenectomy may be curative. This observation has been made repeatedly for cancer of the breast and can be expected to hold for endometrial cancer. Selective lymphadenectomy, or sampling, has disclosed positive nodes in 20 per cent of the patients. The obturator, hypogastric, and iliac nodes were most frequently involved. Perhaps in these patients one should go back and perform a second, more radical operation for removal of the nodes. If the sampling is negative, as it has been in 80 per cent of the patients, nothing further need be done. In other words, why subject all of these patients to radical lymphadenectomy when 80 per cent will not need it?

Last and certainly not least, as pointed out in the article referred to above, if the nodes are positive, then chances are good indeed that there are also coexisting vascular metastases of the endometrial cancer, which probably explains the poor prognosis when the pelvic nodes are positive. The primary cancer may invade vessels of the involved organ or it may develop secondary vascular spread from the metastases in the lymphatic system. Table XV of the article referred to also mentions other cancers of the rectum, bladder, kidney, and endometrium as having frequent vascular metastases.

It is quite likely that the intracavity radium helps to localize the lymphatic and vascular cancer emboli in the uterus and prevent their dissemination during the surgical hysterectomy. That is the only explanation that I have for the slightly better results obtained by Dr. Corscaden in the cases that received preoperative radium. On the other hand, one must bear in mind that primary cancers occurring elsewhere in the body are not usually irradiated prior to the surgical excision.

While it is perfectly proper to estimate prognosis in terms of the treatment employed, another yardstick, such as the stage of the disease at operation, is most important. Such a classification was presented by me in *Cancer*, vol. 5, p. 485, 1952, and approximately 320 of our cases can be classified as follows:

		NO. OF CASES	FIVE-YEAR SURVIVAL
Stage 0	Limited to endometrium	56	75%
I	Limited to uterus	170	
II	Adnexal spread	58	
III	Lymph node metastasis	16*	0%
IV	Carcinomatosis	20	
	Total	320	

*Out of 60 cases so studied.

DR. MICHAEL J. JORDAN.—The incidence of carcinoma of the endometrium is rapidly approaching that of carcinoma of the cervix—approximately 1 case of *corpus* cancer to every 1.5 cases of cancer of the *cervix*.

A series of 420 cases, including early and advanced, untreated, adequately and inadequately treated elsewhere, and then admitted to Memorial Hospital during the years 1935 to 1942, revealed a relative cure rate of 24.8 per cent and a net cure rate of 29.7 per cent.

Of course, the majority of cures occurred in the group that was diagnosed early and treated adequately, i.e., cases localized to the uterus—here the relative cure rate was 63.9 per cent and the net cure rate 83.8 per cent.

After reviewing the records of a large number of cases treated elsewhere and referred to Pondville and Memorial Hospitals, it was observed that the failure to obtain a cure in a large number of cases was due to one or a combination of the following:

1. Diagnosis of carcinoma not established preoperatively.
2. Supracervical hysterectomy done.
3. Inadequate total hysterectomy done with recurrence in rim of cervix, pubocervical fascia, parametria, or uterosacral ligaments.
4. Inadequate vaginal cuff with metastasis to vaginal vault.

One wonders whether a fifth reason should not be added, namely, failure to dissect the pelvic lymph nodes. Perhaps a 6th reason should also be added and that is failure to do a partial or complete exenteration where there is contiguous involvement of the bowel or bladder. Some of these cases have now reached the five-year salvage point.

The approximate incidence of positive nodes in corpus cancer has been established by independent investigation as being 15 to 25 per cent.

Since the finding of a positive lymph node in an early case, seven years ago, I have done a modified radical abdominal hysterectomy with contiguous node dissection on a selected group of 20 cases, with an incidence of positive nodes of 25 per cent.

Three weeks ago when Dr. Meigs visited Memorial Hospital, he told me that of approximately 25 cases of carcinoma of the corpus, operated upon by him, 6 had positive nodes and all these patients were dead.

I am not free to discuss the results of all the 56 cases treated on the gynecological service at Memorial Hospital, but the incidence of positive nodes is within the 15 to 20 per cent range. There was one death from a complication of anesthesia, a mortality rate of 1.7 per cent. The present opinion at Memorial Hospital is that, if possible, the treatment should be the same as that of carcinoma of the cervix. I believe, however, that this procedure should be advocated only on a selected basis because it must be taken into consideration that: (1) these patients are generally in a 10 to 15 year older age group than the cervix cases; (2) there is a higher incidence of complications such as obesity, diabetes, and cardiovascular disease; (3) there is the important added risk of ureteral injury; (4) venous spread may occur in carcinoma of the corpus.

Taking all these risks to increase the over-all salvage by a small percentage does not as yet justify this as a routine procedure.

One must also remember that generally carcinoma of the endometrium metastasizes slowly as compared to carcinoma of the cervix. The broad ligament and ovaries frequently act as a barrier in carcinoma of the endometrium. Unlike the situation with carcinoma of the cervix, a considerable number of patients who die from metastatic carcinoma of the endometrium have no evidence of residual disease in the pelvis. The pelvic lymph nodes may be completely by-passed. Obviously the answer is early diagnosis. Perhaps this can be brought about by regular interval cytological study of endometrial smears on all women after the age of 40.

DR. W. E. STUDDIFORD, JR.—I would like to mention one case that bears out in reverse the statements of Dr. Javert, Dr. Jordan, and Dr. Peightal in regard to the poor outlook of patients with proved lymphatic spread from adenocarcinoma of the corpus. This patient was seen in October, 1953, in the follow-up clinic of Bellevue Hospital. She had been operated on for adenocarcinoma of the corpus following radiation therapy in 1940, 13 years ago. At the time of her visit she showed no evidence of recurrence and appeared to be in perfect health. The operative specimen showed residual adenocarcinoma

of the corpus and a separate node removed from the right parametrium was said to have shown metastatic adenocarcinoma. It seemed so unlikely that this patient would have survived for this period of time with this finding that the sections were reviewed. The diagnosis on the lymph node was found to be in error. It was a clear-cut example of endometriosis.

DR. J. EDWARD HALL.—It is impossible for us to analyze all the figures which Dr. Corscaden has given us. I would like to state for the record, Dr. Peightal, that in your consideration of institutions throughout the country that are treating this disease by radical hysterectomy and widespread node dissection, there should be added the State University in Brooklyn. For the past three years we have been treating these patients, every one of them, by a very radical hysterectomy and node dissection, and some of us are becoming a little discouraged with our results. I would like to bring up one point that has been emphasized by Dr. Peightal, by Dr. Javert, and especially by Dr. Jordan, that the patients with node involvement apparently are doomed. If that is true, are we therefore justified in doing this radical procedure, which bears an increased morbidity with it and also an increased operative mortality?

DR. CORSCADEN (Closing).—What Dr. Hall has emphasized was one point that I was going to emphasize. In these old publications it was not stated that there was no lymph node involvement, but the impression given was that, if those nodes were involved, the disease had gone further. In other words, local lymph node involvment was not a mechanical problem. It was a biological problem.

The worst case I have had was that of a woman who was dead within three months after she had been operated upon. Ten days after her first drop of blood a tiny lesion was found in the uterus. The other extreme was a woman watched for two years with what was thought to be a fibroid, which finally proved to be a mass of carcinoma about 10 cm. in diameter. She lived 20 years and died of another disease. In other words, it is the biological factor that is important. In the rather amusing second slide of the operative cases, 75 per cent of the patients improperly operated upon lived and only 60-add per cent of those properly operated. Apparently, the well-treated cases there were more of these biologically *lethal* cases.

From our information gained from these 250 cases and as a matter of fact backed by another 150 cases of the previous ten years, I can see only that about 5 per cent of cancers localized to the endometrium are of this lethal type. Dr. Hall and Dr. Jordan objected to the proposal that radical hysterectomy be the routine therapy. I do not think Dr. Javert or Dr. Peightal have that thought in mind at all. Those who have the facilities, the blood banks, etc., should pursue this question of the importance of metastases to the local lymph nodes and answer it by an accumulation of knowledge. But we should teach, I believe, what seemed to appear in our experience. If you diagnose early, and can get these cases while the gross lesion is limited to the endometrium, you are going to cure close to 90 per cent. The routine should be just as it is now. I won't urge the radium. I think it is better in the bulky, massive, obvious cancers of the uterus. I do believe that the extended operation will have a high mortality. In the cases here presented it was 2 out of the 251 cases. Both had coronary occlusion, both on the seventeenth postoperative day. I do not believe these arteriosclerotic, obese women will withstand the extended operation. To recapitulate, the investigators should pursue the search for lymph nodes but the routine procedure for the common lot of us should be an adequate hysterectomy, preceded, in the bulky cancers, by radium.

PREINVASIVE CARCINOMA OF THE CERVIX

Correlation of Findings in Biopsy and Hysterectomy Specimens

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PAUL KIMMELSTIEL, M.D., CHARLOTTE, N. C.

(From the Presbyterian and Charlotte Memorial Hospitals)

A SHARP rise in the incidence of preinvasive carcinoma of the cervix has been experienced in this community since cytologic studies of vaginal smears have been carried out as a routine procedure in the examination of a large segment of the female population. Adequate treatment of this form of cancer has, therefore, become a major problem.

Even though we are uncertain of the course of carcinoma in situ* if left alone, we are compelled to direct our treatment toward complete eradication of this lesion, since a small, but significant, number of intraepithelial carcinomas are known to have progressed eventually into the infiltrating and metastasizing type. Total hysterectomy appears to be the most widely accepted treatment. Yet, purely local treatment of the cervix is believed by some[8, 10-14] to be sufficient, since the lesions are so frequently confined to small areas at the squamocolumnar junction, and because remaining or recurrent foci can readily be detected by subsequent vaginal smears.

It appears to us that a study of total uteri at various intervals following different types of biopsies and treatments prior to hysterectomy may shed light upon the frequency of residual carcinoma in the remaining uterus and the conditions under which it may be expected. Such knowledge may be helpful in determining proper management of these cases.

Material and Methods

From 1949 through 1952, 95 cases of in situ cervical carcinoma were found in the files of the Department of Pathology of the Charlotte Memorial Hospital and the Presbyterian Hospital. Since the object of this study is to correlate the findings in the cervical biopsies with those of subsequent hysterectomies, 24 cases had to be rejected. In 2 of the 24 cases the lesion was treated with irradiation prior to hysterectomy; in 8 of them no hysterectomy was performed after the diagnosis was established by biopsy; and in 14 instances, the in situ carcinoma was discovered incidentally in uteri removed for other reasons. This left a total of 71 cases in which both biopsy and hysterectomy specimens were available for examination.

Parallel to this study, all cervices received from the operating room were routinely examined by the multiple-block method to determine the frequency of clinically unrecognized in situ carcinoma of the cervix. Six blocks were taken across the squamocolumnar junction in such a manner that ample portio and inner cervical mucosa were present. If malignancy was questioned, the

*The terms carcinoma in situ, preinvasive and intraepithelial carcinoma are used synonymously.

entire mucosa with ample underlying stroma at this site was embedded in a sagittal fashion. More recently we have on occasion embedded the entire upper cervical mucosa as well.

The morphologic criteria used in this study for the diagnosis of intraepithelial cervical carcinoma are those generally accepted. A clear and detailed discussion can be found in Stoddard's monograph[8] and need not be repeated here. An occasional case of atypical hyperplastic epithelium may be difficult to distinguish from in situ carcinoma. These "borderline" incidences have been excluded from the study. All cases were examined by 2, often by 3, pathologists, who concurred in the diagnosis. Infrequently, there was not complete agreement in regard to "beginning penetration" or "early invasion," but disagreement was often resolved by serial histologic sections. We should state that we do not recognize glandular involvement as infiltration since the continuous physiologic barrier, i.e., the so-called basement membrane, remains intact. Stoddard and his associates have pointed out that the immediate juxtaposition of cells of the Malpighian layer to connective tissue in penetrating pegs can be used as a helpful criterion for early invasion. We have found this to be true. Nevertheless, there remained 2 cases in which we were not able to define clearly whether a minute focus of penetration of the basement membrane existed. Since these were quite superficial and all 3 pathologists agreed that the evidence for invasion was disputable, the cases were included in this series.

We have attempted, where technically possible, to estimate crudely the extent of the lesion and also the glandular involvement. The latter was classified as minimal, moderate, marked, or absent. Such estimates are possible only with adequate material, such as the whole cervix or a sufficiently large cone biopsy. Further, we tried to predict from the more adequate biopsies whether residual tumor may be anticipated in the subsequent complete hysterectomy specimen. A search was included for multiple or "skip" lesions, or origin of the neoplasm within glandular epithelium. Finally, we sought evidence of neoplasia in regenerating epithelium covering the biopsy defect in complete hysterectomy specimens after an earlier biopsy.

Analysis of Cases

1. Incidence.—

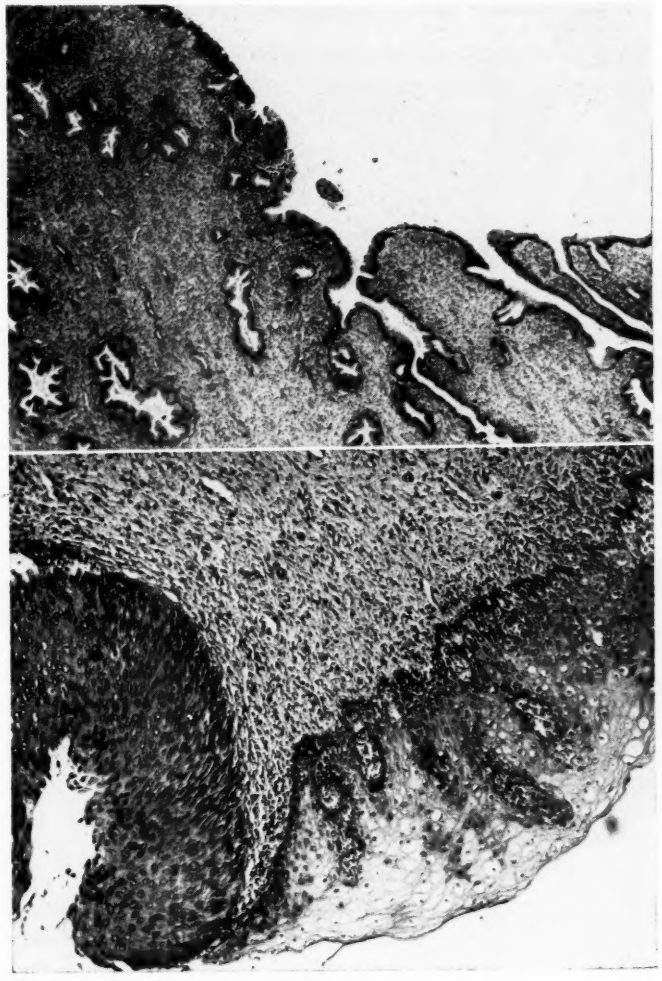
The average age of 71 patients available for study was 37.5 years. The youngest patient was 20 years old and the eldest 61 years old. Twenty-one patients were in the third decade of life and 31 were in the fourth decade.

Although the material did not derive from any single private or group practice, the statistical survey has shown that the number of cases diagnosed as carcinoma in situ has risen parallel to the volume of vaginal smears screened for cancer cells. Only fourteen of 95 cases (14.7 per cent) were found incidentally in uteri removed for other reasons. In the vast majority of the remaining 83 cases (85.3 per cent) one or more positive smears constituted the indication for biopsy. Chronic cervicitis was the most common initial clinical impression, but in many cases a routine vaginal smear revealed the presence of cancer cells in a normal-appearing cervix. In only 1 case was the biopsy performed because of a group of atypical cervical cells which were noted in endometrial curettings.

Thus, in this series, carcinoma in situ was recognized 7 times as often with the aid of vaginal smears as it was detected incidentally. This cannot

be attributed to chance, since all cervices removed during the same period of time were carefully searched for cancer, irrespective of age group of reasons for hysterectomy. The greater frequency, therefore, with which carcinoma in situ was recognized is a direct result of our method of detection and the respectively increased alertness of the public and the medical profession.

A.



B.

Fig. 1.—(P-1052-52.) Example of adequate thick-cone biopsy, *A*, representing the upper margin with normal inner cervical mucosa, *B*, showing clearance of lower margin by normal portio epithelium.

2. Type of Biopsy and Residual Carcinoma.—

Twenty-five of the 71 cases analyzed revealed residual carcinoma in the uterus removed subsequent to biopsy (35.2 per cent). The frequency with which residual tumor was found was dependent to some extent on the type of biopsy. In one group of 38 cases with small or superficial biopsies, residual

carcinoma was found in 16 instances (42 per cent) as contrasted to a second group of 33 cases with large, thick-coned biopsies in which only 9 hysterectomy specimens showed residual tumor (27 per cent). The first group included punch biopsies, small wedge biopsies, and dissection of a superficial mucosal ring. These biopsies disclose little more than the fact that the tumor is present upon the surface or within a few glands included in the fragments. Their small size precludes an estimate of the extent to which the surface and glands are involved.

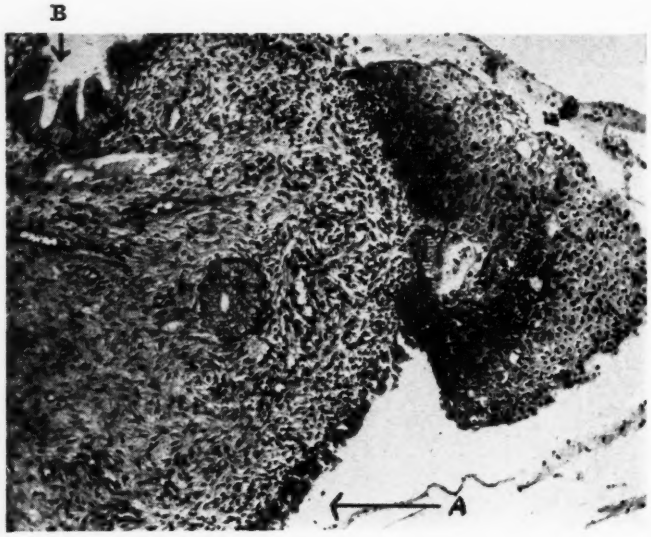


Fig. 2.—(S-2601-52.) At the tip of a fold of the inner cervical mucosa is found a small area of in situ carcinoma. The adjacent cervical mucosa at *A* and *B* is lined by normal cylindrical epithelium.

In most cases a sufficiently large, thick cone permits a reasonably accurate prediction as to whether the tumor has or has not been completely removed. In all of the large type biopsies in which residual tumor was found, the lesion could be seen to extend to the edge of the resection. In those in which normal mucosa was present in the extremities of the biopsy, no residual tumor was detected. However, the absence of carcinoma at the very end of the resected specimen is no absolute guarantee that the tumor is completely removed, for irregular serpiginoid borders and tonguelike extensions may readily be overlooked unless all of the material is serially sectioned. Occasionally, though infrequently, isolated islands of carcinoma were observed at some distance from the major tumor field, separated from it by normal mucosa. We observed two such instances. Whether these findings are interpreted as portions of irregular extensions or as being of multicentric origin does not alter the fact that they may occur beyond the boundaries of the excised, apparently normal mucosa in he biopsy. Yet our own experience with 33 cases of adequate thick-cone biopsies indicates that the presence or absence of tumor in the remaining uterus can be predicted with reasonable accuracy.

Such appraisal is obviously impossible in most cases of small biopsies. Proper evaluation of these is also greatly impaired by technical difficulties

which should not be underestimated. Many of these tissue fragments do not permit an orientation of the block perpendicular to the mucosal surface. Traumatic damage increased in direct proportion to the smallness of the biopsy. There were 12 instances of small biopsies in which no residual tumor was found. This could not be predicted in 8 of these since only fragmentary portions of the surface epithelium were visualized. Even serial sections would

Fig. 3.

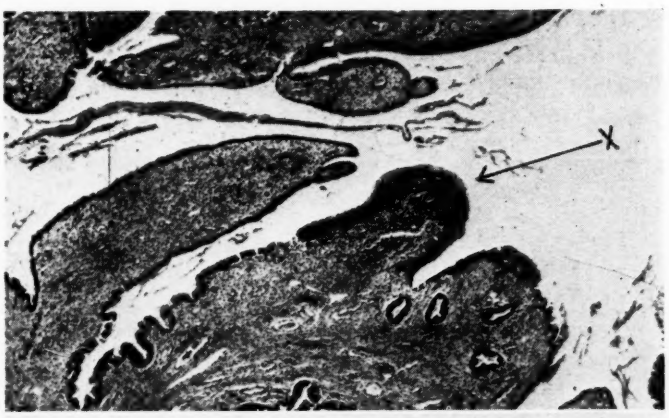


Fig. 4.

Fig. 3.—(S-2601-52.) Skip lesion. In another portion of the same inner cervical canal is found a small area of in situ carcinoma (*X*). The surface above and below is lined by normal inner cervical mucosa.

Fig. 4.—High-power magnification of the area of carcinoma in situ (*X*) in previous Fig. 3.

not have yielded indisputable evidence one way or another. In 4 of these 12 cases, however, the tumor extended to the edge of the resection and residual carcinoma should have been predicted. Yet, no residual tumor was found. Aside from the previously mentioned technical factors, it is reasonable to assume that all of the remaining small tumor was destroyed as the result of the operative procedure.

3. Glandular Involvement.—

The extent of glandular involvement could be fairly well estimated in thick-cone biopsies. In small ones the hysterectomy specimen had to be correlated in order to accomplish such estimate. Without consideration of the grading to which we previously referred, we found at least minimal, but definite, involvement of glands in 65 of the 71 cases (91.5 per cent). We have no explanation as to why the frequency in our series is so much higher than that of others[5, 15] unless quantity enters into the definition of criteria. This problem was not pursued, however, because we could not establish a definite correlation between the degree of glandular involvement and the surface extension of the lesion, nor could we correlate it to the age of the patient.

Fig. 5.

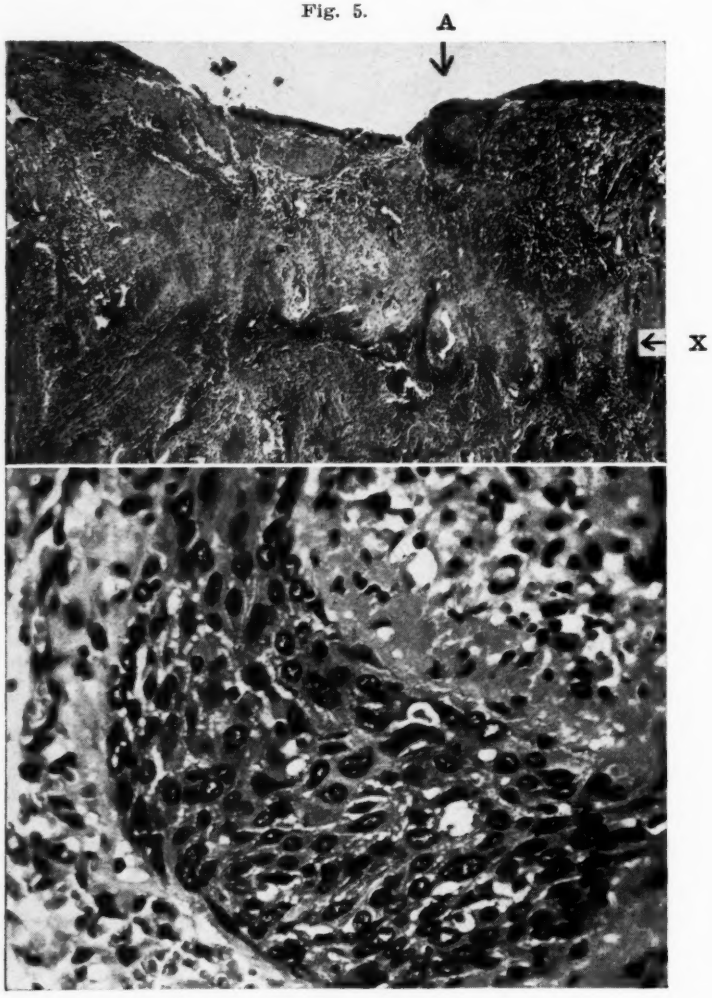


Fig. 6.

Fig. 5.—(S-164-53.) Cervix approximately three weeks postbiopsy. A deep zone of necrosis and hyalinization is seen, the deepest margin of which is indicated by *X*. The surface is lined by nonkeratinizing stratified squamous epithelium, covering the defect by centripetal growth. The deep underlying zone of necrosis is evidence of the fact that the epithelium is recently formed. At *A* an atypical penetrating peg is found.

Fig. 6.—High-power magnification of epithelial peg in Fig. 5 (*A*). The atypicality of epithelium is indicated by variation in size and staining effect of nuclei, some of which are large and hyperchromatic.

4. Recurrence in Regenerating Epithelium.—

If endocrinological or other systemic disorders play a part in the development of cervical carcinomas, one should expect to find their origin not only in pre-existing mucosa but also, and particularly, in regenerating epithelium covering the site of previous biopsies in which small carcinomas have been completely removed. There are many reasons why a proof of such hypothesis encounters extreme difficulties. Although we have not been able to demonstrate a carcinoma arising in regenerating epithelium in our studies of post-biopsy uteri, we have found 1 case in which the atypicalities of regenerating surface epithelium strongly suggest anaplasia. The case is included in this report to stimulate further search. Even exceptional observations of carcinomas at such sites would be of great practical and academic value. (Illustration, description.)

Comment

It is generally agreed that preinvasive carcinoma has its origin in the vicinity of the squamocolumnar junction of the cervix.[1-6] From this initial field the tumor spreads circumferentially, longitudinally, and into the glands.[7] As the disease progresses, it successively involves the surface epithelium of both portio and inner cervical mucosa, the endocervical glands, and finally the stroma.[1, 2, 4] It has been suggested that one to twelve years is required for the complete unfolding of this process.[8]

Investigation of these lesions should, therefore, be directed toward this critical area. In agreement with many others,[8-10] our own study has led us to conclude that adequate investigation of this area is possible only with the thick-cone biopsy. The cone should be removed by scalpel, without cautery, generously encircling the squamocolumnar junction and should include approximately 2 cm. of the endocervical canal.[8]

This procedure will not interfere with future childbearing. It requires hospitalization, however, and entails the danger of postoperative hemorrhage and cervical stricture. These disadvantages must be weighed carefully against the advantages which this method has over small spot biopsies. It is apparent that this technique is justified only if there is strong suspicion of an existing carcinoma. In that case, however, it is the only method, short of cervical amputation or hysterectomy, which will allow adequate appraisal of extent and possible invasion of an existing lesion. Any of the small superficial biopsies is inadequate for this purpose. They should be used only to establish the existence or absence of carcinoma in a grossly recognizable lesion of the cervix.

Biopsies other than those of the thick-cone type have no place in the recognition of treatment of suspected preinvasive carcinoma of the cervix. In the first place, negative findings in spot biopsies do not rule out cancer in the face of positive vaginal smears or strong clinical suspicion. In the second place, if in situ carcinoma is present, such biopsies must be supplemented by large-cone biopsies for the purpose of mapping the lesion.

The method of vaginal smear screening, if properly conducted, is sufficiently reliable to give adequate indication for large-cone biopsy. The ac-

curacy of this method on the positive side ranges between 96 and 98 per cent. Thus, if cancer cells are found, or even if repeated smears are reported as being only highly suspicious, a full biopsy is justified and is, under such circumstances, the procedure of choice.

Our own study has shown that the surface extent and depth of cervical lesions can be determined in this manner with a great degree of certainty. If the lesion is found to be small and apparently completely excised, the biopsy may be regarded as the definitive treatment of choice. The chance of missing small irregular extensions or multiple lesions does not appear significant but its very possibility makes a follow-up study by vaginal smear mandatory.

Summary

A series of preinvasive carcinomas of the cervix was analyzed relating the type of biopsy to the findings in subsequently removed uteri. It is concluded that:

1. The thick-cone biopsy is the method of choice in every case with a positive vaginal smear or clinical suspicion of cancer. Small or superficial biopsies have no place in the recognition or treatment of suspected early cancer of the cervix.

2. The thick-cone biopsy permits reasonably accurate mapping of the lesion and may, therefore, determine the type of definitive treatment.

3. In selective instances the thick-cone biopsy may by itself constitute definitive treatment, but should then be followed by periodic vaginal smears.

References

1. Te Linde, R. W., and Galvin, G. A.: Am. J. Obst. & Gynec. **48**: 774, 1944.
2. Ulfelder, H.: Bull. New England M. Center **11**: 159, 1949.
3. Galvin, G. A., and Te Linde, R. W.: Am. J. Obst. & Gynec. **57**: 15, 1949.
4. Hertig, A. T., and Younge, P. A.: Am. J. Obst. & Gynec. **64**: 807, 1952.
5. Foote, F. W., and Stewart, F. W.: Cancer **1**: 431, 1948.
6. Wollner, A.: Surg., Gynec. & Obst. **68**: 147, 1939.
7. Pund, E. R., Nettles, J. B., Caldwell, J. D., and Nieburgs, H. E.: Am. J. Obst. & Gynec. **55**: 831, 1948.
8. Stoddard, L. D.: Progress in Fundamental Medicine, Philadelphia, 1952, Lea & Febiger.
9. Carter, B., Cuyler, K., Thomas, W. L., Creadick, R., and Alter, R.: Am. J. Obst. & Gynec. **64**: 833, 1952.
10. Peightal, T. C.: In discussion of Carter, B., Cuyler, K., Thomas, W. L., Creadick, R., and Alter, R.: Am. J. Obst. & Gynec. **64**: 833, 1952.
11. Martzloff, K. H.: In discussion of McKelvey, J. L.: Am. J. Obst. & Gynec. **64**: 816, 1952.
12. Davis, C. H.: In discussion of Carter, B., Cuyler, K., Thomas, W. L., Creadick, R., and Alter, R.: Am. J. Obst. & Gynec. **64**: 833, 1952.
13. Pund, E. R., and Echols, J. M.: J. A. M. A. **143**: 1226, 1950.
14. Hoge, R. H.: Obst. & Gynec. Surv. **5**: 621, 1950.
15. Younge, P. A., and Hertig, A. T.: Am. J. Obst. & Gynec. **58**: 867, 1949.

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AN EVALUATION OF STAINING TECHNIQUES FOR DEMONSTRATION OF POLYSACCHARIDES AND NUCLEOPROTEINS WITH SCHIFF (FUCHSIN SULFUROUS ACID) REACTIONS IN CANCER CYTOLOGY*†

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(From the Cancer Institute at Miami)

THE modified Best carmine stain for glycogen uses a staining of nuclei with hematoxylin and a carmine stain for the cytoplasm of cells. This method, which gives valuable information for physiologic and pathologic purposes, such as sexual maturity, level of ovarian functions, estrogen content, cancer, etc., is used routinely.[1, 2, 3, 4]

Two other methods suitable for demonstration of polysaccharides are the lead-tetra-acetate-Schiff reaction by Criegee[5] (1931) and the periodic-acid-Schiff method of McManus[6] (1946). These methods have not yet been used generally in clinical cytology.

The periodic-acid-Schiff technique is believed to involve two chemical reactions: (a) an oxidation of 1-2 glycols and a- amino alcohol groups with periodic acid to produce aldehyde groups; and (b) a reaction of these aldehyde groups with the Schiff reagent (fuchsin sulfurous acid) to produce a red color. We performed the reaction also with lead-tetra-acetate, a reagent with similar oxidative properties, to see whether the results were comparable.

Cytology

Following the technique of the carmine stain the nuclei of vaginal epithelium are not stained. Just around the nuclei the concentration of carmine granules may be found very intense, resulting in big clumps of carmine in the center of the cell now and then, simulating a nuclear staining, but the nucleus itself does not seem to be stained (Fig. 1). In the Best carmine stain technique, therefore, the nuclei are first stained with hematoxylin. By this method, cornified cells contain a great amount of glycogen. Precornified cells with vesicular nuclei usually contain less glycogen, although there are exceptions to this rule. Precancer and cancer cells contain no glycogen at all, like parabasal cells (Fig. 2).

There is a great contrast between the coloring properties of cells stained with carmine for glycogen and those stained with periodic-acid-Schiff or lead-tetra-acetate-Schiff. In the latter stain, cornified superficial squamous cells show only a very faint red color in their cytoplasm. The pyknotic nucleus is

*This work was supported by a research grant from the National Cancer Institute of the National Institutes of Health, United States Public Health Service.

†Presented at the forty-seventh annual meeting of the Southern Medical Association, Atlanta, Oct. 26, 1953.

Fig. 1.

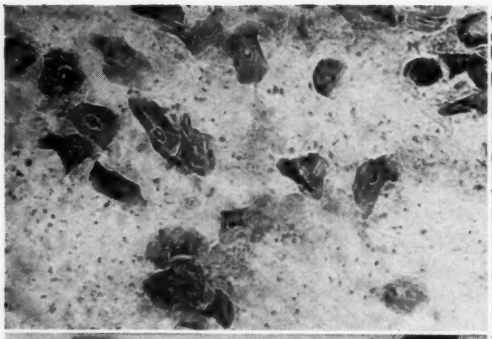
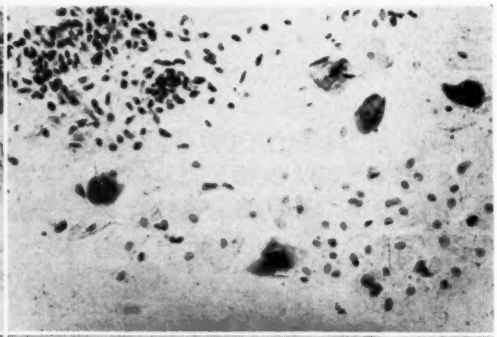


Fig. 2.



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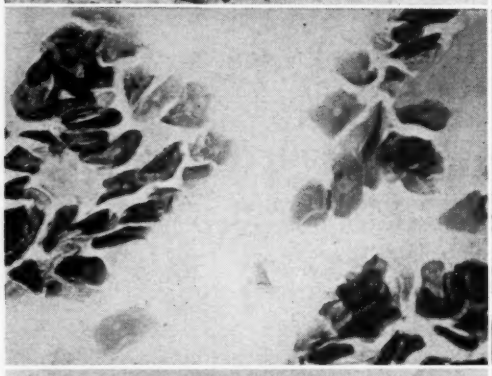


Fig. 4.

Fig. 5.

Fig. 6.

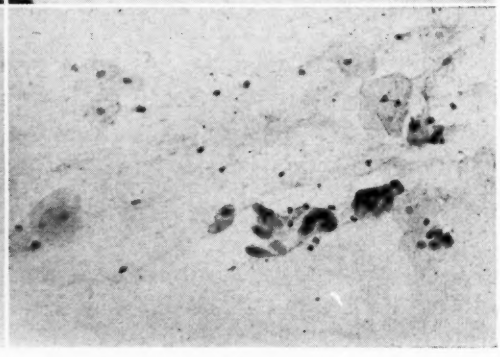


Fig. 1.—Best carmine stain. Normal superficial squamous cells from cervical scraping. Nucleus not stained. Concentration of carmine granules in clumps around the nucleus. (×150; reduced ⅙.)

Fig. 2.—Best carmine stain with hematoxylin counterstain. Normal precornified cells, right bottom, do not contain glycogen or only little, nor do the precancer cells, upper left, whereas the cornified cells contain much glycogen. (×150; reduced ⅙.)

Fig. 3.—Lead-tetra-acetate-Schiff procedure without hematoxylin counterstain. Cornified cells show only a faint red color. Precornified cells show an intense staining with heavily stained borders. Nucleus not stained. (×150; reduced ⅙.)

Fig. 4.—Lead-tetra-acetate-Schiff technique with hematoxylin counterstain. The precancer cells in the center and right and the precornified cells at the left and the right show more stain in their cytoplasm than the cornified cell at the right above the precancer cells. (×150; reduced ⅙.)

Fig. 5.—Lead-tetra-acetate-Schiff stain with hematoxylin counterstain. Precancer cells right at the bottom show more staining of the cytoplasm than the cornified cells. (×600; reduced ⅙.)

Fig. 6.—Lead-tetra-acetate-Schiff technique with hematoxylin counterstain. Endocervical cells in the center show greatest staining intensity due to their content of mucoproteins. The precornified cells dispersed through the picture show more stain in the cytoplasm than the cornified cells just above the endocervical cells. (×150; reduced ⅙.)

not stained or very slightly and is hardly visible. The border of the cell is also faintly colored. Precornified cells show more staining intensity in their cytoplasm. Again the nucleus is hardly stained. Now and then it seems as if the concentration of red color around the nucleus is slightly more pronounced, simulating a nuclear staining. The borders of precornified cells are thicker, much more marked, and stain in bright red colors (Fig. 3). The parabasal and basal cells show in general an intense staining along their borders, but because the nucleus in parabasal and basal cells occupies a great deal of the cell, the rest of the cell takes only a light appearance. Cancer cells show slightly more staining quality in their nuclei. Yet for routine examination of cancer cells the staining of the nuclei is insufficient and additional nuclear staining was found to be necessary by hematoxylin or Schiff. Cytoplasm of cancer cells, as of basal cells, stains brightly (Figs. 4, 5). Leukocytes show only faint staining. The greatest staining qualities we find in endocervical cells. Especially the proximal part of the cell stains very intensely, due to its contents of mucoproteins (Fig. 6).

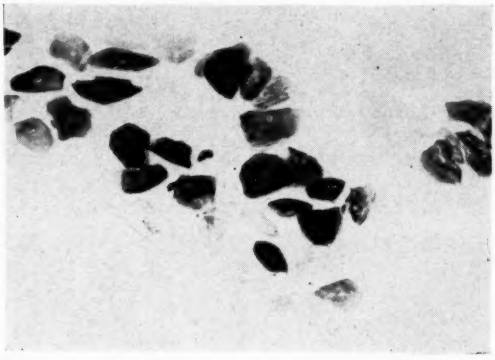


Fig. 7.—Periodic-acid-Schiff technique without counterstain. Cornified cells are slightly stained. Precornified and parabasal cells are very intensely stained though their borders are less pronounced than with the lead-tetra-acetate procedure. Nucleus not stained. (×150; reduced ⅙.)

The cytologic picture, with the use of the periodic-acid-Schiff stain is more or less the same. As with the lead-tetra-acetate staining, the cells show a decreasing stain intensity in the cytoplasm from the basal to the superficial cells (Fig. 7). The cornified superficial squamous cells show only a very faint red color. The pyknotic nucleus is hardly visible and takes a very light red or no stain. The border of the cell is faintly stained. The precornified and basal cells, however, are more intensely stained with this method than with lead-tetra-acetate. The reason why periodic acid as a rule stains more heavily than lead-tetra-acetate is that periodic acid could cleave some protein structures as serine and threonine to leave an aldehyde group at the end of the protein chain; lead-tetra-acetate cannot do that. The lighter background seen in the slides stained with lead-tetra-acetate may be due to nonstaining of these proteins. Nuclei in general are poorly stained and without additional staining with hematoxylin or Schiff, this procedure is not suitable for routine

examination of cancer cells. It is because the part of the cytoplasm adjacent to the border of the nucleus is most heavily stained that it seems now and then (depending upon the plane of the nucleus) that the nucleus itself is stained.

The substances with radicals capable of reacting with periodic acid to produce aldehyde groups are: polysaccharides, glycogen, starch and cellulose, mucopolysaccharides, chondroitin sulfuric acid, chitin, mucoproteins (endocervical cells), mucin, and some other proteins.

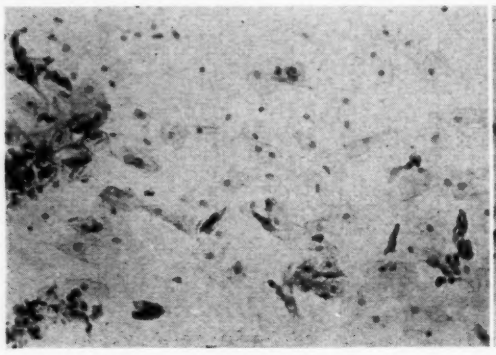


Fig. 8.

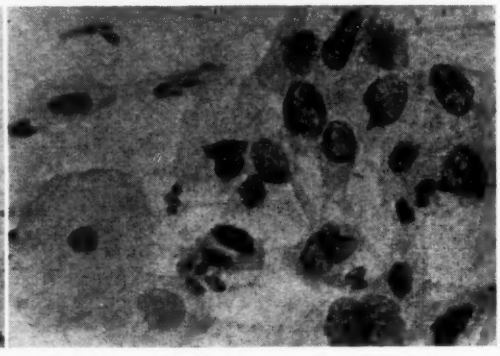


Fig. 9.

Fig. 8.—Dual Feulgen staining. Precancer cells at the left and bottom. Normal precornified cells prevail in the rest of the picture. (×150; reduced ⅙.)

Fig. 9.—Dual Feulgen staining. Precancer cells at the right. A cornified cell at the left. (×600; reduced ⅙.)

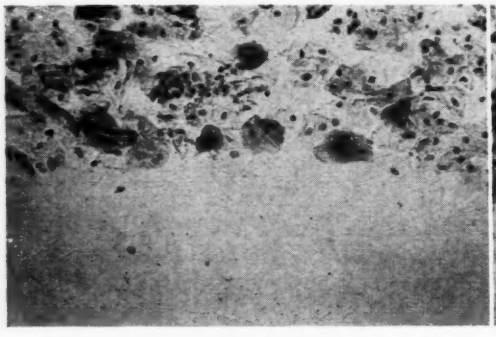


Fig. 10.

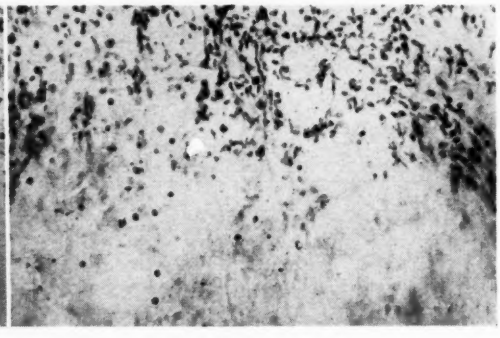


Fig. 11.

Fig. 10.—Carmine staining procedure with counterstain. Amylopsin digests the cells below the midline of the slide. Only cell shadows appear on the lower part of the slide. (×150; reduced ⅙.)

Fig. 11.—Dual Feulgen staining. Amylopsin digests the cells below the midline of the slide. Only cell shadows appear on the lower part of the slide. (×150; reduced ⅙.)

The dual Feulgen stain, composed of the Schiff stain of desoxyribose of the nucleus following hydrochloric acid hydrolysis of the nucleoproteins and the Schiff stain of polysaccharides of the cytoplasm following lead-tetra-acetate oxidizing, combined together, proved a very effective staining method for cancer cells (Figs. 8 and 9). Both red stains of nucleus and cytoplasm left enough differentiation for cancer diagnosis.

The enzyme amylopsin was not able to make differentiations between glycogen and polysaccharides stained either with carmine or with lead-tetra-acetate-Schiff. A slide exposed to amylopsin along half of its width, then stained with any of these methods, shows a digesting of the cytoplasm of the cells just below the midway line (Figs. 10 and 11).

There was a remarkable difference in staining properties between slides stained with lead-tetra-acetate at room temperature followed by Schiff and lead-tetra-acetate at 70° F. followed by Schiff. In the latter case the cornified cells showed a strong red color, precornified and parabasal cells a weak red stain, just as with the carmine method. It is probable that with higher temperatures glycogen is more readily stained than with a low temperature, observations which are in accordance with those of Glegg and associates.[7] Cervical cells containing mucoproteins and stained strongly when oxidized with

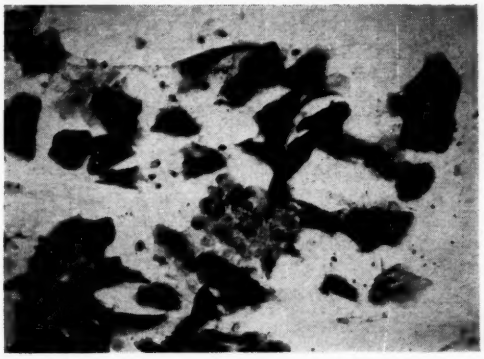
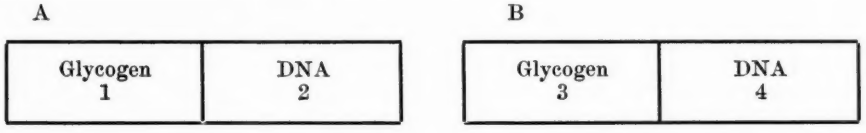


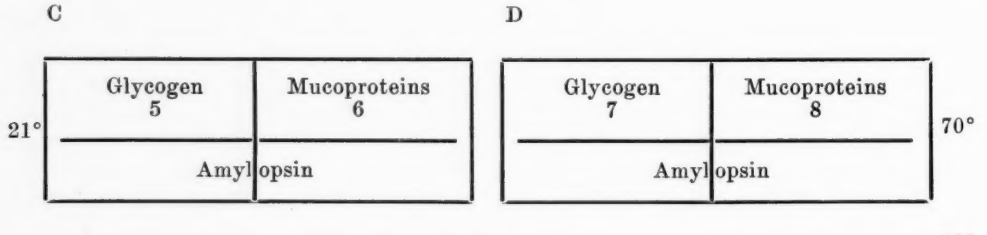
Fig. 12.—Lead-tetra-acetate Schiff with counterstaining. At a temperature of 70° F., cornified cells contain much stain intensity due to high content of glycogen. Precornified cells, upper left and low right, and the mass of endocervical cells in the center contain only little stain. (×150; reduced ⅙.)

lead-tetra-acetate at room temperature were stained much less red when oxidized at 70° F. (Fig. 12). To make the cell reactions understandable the following experiments were taken in vitro:



Take two slides, A and B. To take care that substances stick to the glass, albumin was smeared over both slides in equal thickness. Before any experiment was made it was determined that albumin itself did not stain with any of the mentioned stains. On the left half of slide A, glycogen was smeared; on the right half, desoxyribose nucleic acid. The same procedure was performed on slide B with the same quantities of material. Slide A was stained with carmine stain. Slide B was stained with lead-tetra-acetate-Schiff. The results were:

Glycogen 1 ---------- red
DNA 2 ---------- no color
Glycogen 3 ---------- red
DNA 4 ---------- no color



Take two slides, C and D. On the left half of slide C glycogen was smeared, on the right half mucoproteins. The same procedure was performed on slide D with the same quantities of material. Half of both slides were exposed to amylopsin. The materials on the slide were then oxidized by lead-tetra-acetate, slide C at normal temperature, slide D at 70° F. Both slides were then treated with Schiff. The results were:

Glycogen 5 ---------- slightly red
Mucoproteins 6 ---------- dark red
Glycogen 7 ---------- dark red
Mucoproteins 8 ---------- slightly red
Amylopsin ---------- no stain

Methods and Chemistry

The methods used for periodic acid were identical to those described in *Stain Technology*[7, 8, 9, 10] and other papers. We used the following methods:

1. Oxidize the slide in periodic acid for 10 minutes.
2. Wash in 70 per cent alcohol for 5 minutes.
3. Stain in Schiff reagent for 45 minutes.
4. Wash in three changes of potassium metabisulfite water for 5 minutes each.
5. Dehydrate and mount in Canada balsam. Control slides were not oxidized with periodic acid.

The nature of the chemistry of periodic acid and glycols to produce aldehyde groups could be understood as described by Glegg.

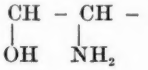
$$R - \underset{\underset{OH}{|}}{CH} - \underset{\underset{OH}{|}}{CH} - R' + HIO_4 = R\underset{\underset{O}{\|}}{CH} + R'\underset{\underset{O}{\|}}{CH} + HIO_3 + H_2O$$

For amino alcohols ($R - \underset{\underset{OH}{|}}{CH} - \underset{\underset{NH_2}{|}}{CH} - R'$) comparable reactions are described. The staining with lead-tetra-acetate proceeds as follows: (in accordance with Hashim and Acra[9]).

1. Fix the slide in 80 per cent alcohol 15 minutes or more.
2. Bring in alcohol 100 per cent 2 minutes.
3. Place in toluene solution 2 minutes.
4. Bring in lead-tetra-acetate solution in toluene 5 minutes.
5. Rinse in three successive alcohol washings 100 per cent, 90 per cent, 70 per cent.
6. Bring in H_2O 2 minutes.
7. Place in ethylene diamine tetra acetate (EDTA) 2 per cent to remove excess reagent 5 minutes.
8. Bring in distilled water two rinses of 2 minutes.
9. Place in leukofuchsin 20 minutes.
10. Rinse for 3 successive 10 minute treatments in acid sulfite solution.
11. Bring in tapwater 3 minutes.
12. Rinse in distilled water 3 minutes.
13. Dehydrate in alcohol 70 per cent, 90 per cent, and 100 per cent and xylene.
14. Mount.

The nature of the chemistry of lead-tetra-acetate with glycols to produce aldehyde groups could be understood by the following reactions:

For amino alcohols (R – CH – CH – R′) comparable reactions are described.



Solutions

1. Periodic acid: 0.8 Gm. in 20 ml. of distilled water; 10 ml. of 0.2 M sodium acetate and 70 ml. of ethyl alcohol were added.
2. Schiff reagent was prepared as described by Longley.[11]
3. Sulfite water is composed of 5 ml. 10 per cent postassium metabisulfite (or sodium metabisulfite), 5 ml. normal hydrochloric acid in 100 ml. distilled water.
4. Lead-tetra-acetate: A 0,023N lead-tetra-acetate solution in toluene. This solution was prepared from a stock solution, a saturated lead-tetra-acetate solution in glacial acetic acid.
5. Ethylene diamine tetra-acetic acid (EDTA) solution: A 2 per cent solution of EDTA was prepared with the aid of gentle heat and the requisite amount of 1N NaOH to bring the solution to pH 8.
6. Amylopsin: 0.2 Gm. amylopsin in 100 c.c. of solution at pH 7.

Conclusions

This report describes different Schiff techniques for staining the nuclei and cytoplasm of cancer cells and compares this with the carmine stain.

References

1. Mapleson, P.: Canad. Tech. J. **2**: 166, 1949.
2. Ayre, W. B., and Ayre, J. E.: Am. J. Clin. Path. **20**: 644, 1950.
3. Hopman, B. C.: AM. J. OBST. & GYNEC. **65**: 1228, 1953.
4. Papanicolaou, G. N., Traut, H. F., and Marchetti, A.: The Epithelia of Women's Reproductive Tract, New York, 1948, The Commonwealth Fund, pp. 30-38.
5. Criegee, R.: Angew. Chem. **53**: 321, 1940.
6. McManus, J. F. A.: Stain Technol. **23**: 99, 1948.
7. Glegg, R. E., Clermont, Y., and Leblond, C. P.: Stain Technol. **27**: 6, 1952.
8. Hashim, Sami, A., Acra, Aftim, N., Afifi, Adel K., and Shanklin, William M.: Stain Technol. **28**: 3, 1953.
9. Hashim, Sami A., and Acra, Aftim, N.: Stain Technol. **28**: 1, 1953.
10. Lhotka, John. F.: Stain Technol. **27**: 213, 1952.
11. Longley, J. B.: Stain Technol. **27**: 161, 1952.

WHAT CAN SURGERY ACCOMPLISH IN RECURRENT CARCINOMA OF THE CERVIX?*

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WITH the renaissance of interest in the surgical treatment of cancer of the cervix the question naturally arises as to the efficacy of surgical attack in comparison with radiation. The answer will not be readily forthcoming as considerably more patients treated surgically will have to be observed for five years or more than is possible at present. However, there is another aspect of the problem deserving attention and that is the problem of the patient who has received radiation therapy and presents recurrence or persistence of disease. Since the best radiation results now reported claim a 40 per cent over-all "cure" rate, it is inferred that 60 per cent of patients will eventually come into the group of recurrent cases. Of course many of these will present widespread dissemination and therefore will be beyond hope of "cure" by any method of local treatment. On the other hand, a number of these patients will present recurrences still limited to the pelvis and for these the problem arises as to re-radiation or some other form of treatment.

In general, re-radiation is not regarded as curative for recurrences, and should not be advised, although re-radiation may have value as palliative treatment. There have been some exceptions to this point of view and certain authors claim successful control of recurrences by re-radiation. The weakness of their claim, however, lies in the fact that in many instances recurrences are diagnosed simply upon pelvic examination and the detection of areas of induration that have not been previously found present. Very often no biopsy is reported to confirm the presence of recurrences. Thus it is not certain but that many of these successes were in reality instances of inflammation that eventually regressed or remained stationary. In his excellent work on uterine cancer, Truelsen[3] found that, of 390 patients whose lesions did not disappear after six months following radium therapy, 100 per cent were dead at the end of two years. Among 216 patients who exhibited local recurrences six or more months after apparent healing following radium therapy, 63 showed apparent healing after a second radium treatment, but, of these, 51 patients were dead by the end of the third year following the second treatment—a survival rate of 5.5 per cent (of the 216 patients) for three years. Of the 390 patients who did not heal primarily plus the 216 patients who received re-radiation after they apparently healed once, the over-all survival rate for three years was 12 patients, or 1.7 per cent. Obviously this is a low salvage rate.

*Address delivered before the Forty-third National Congress of the Italian Society of Obstetrics and Gynecology, Rome, Sept. 22, 1953.

Besides re-radiation, the only other method of treatment conceivable at this time for recurrences of cancer of the cervix after radiation failure is surgery. The purpose of this report, therefore, is to present the results of a surgical program in attacking recurrent cancer of the cervix.

In a series of 416 patients with carcinoma of the cervix in all stages seen in the Gynecological Service of the Memorial Hospital from Sept. 7, 1947, to Dec. 31, 1949, the policy was to consider every patient a surgical problem and to advise operation whenever possible. In 48 patients an exploratory laparotomy or only a palliative excisional procedure was carried out because of the advanced stage of the disease. One hundred patients were not operated upon for a variety of reasons, including refusal on the part of the patient (11); patients apparently cured by radiation elsewhere and registered in the service for follow-up (19); operated upon elsewhere (4); not operated upon and lost to follow-up (5); received preoperative therapy in limited doses and failed to return (20); private patients of staff members who elected to treat by radiation (10); and, considered very poor operative risks or had extrapelvic metastases evident upon clinical examination (31). This detailed account of the patients not operated upon in this group is presented in order to demonstrate that the patients with recurrent cancer of the cervix who were opreated upon were not selected patients with recurrences but represented all such patients who were observed among the 416 who presented themselves who did not exhibit extrapelvic metastases.

Among the 268 (of 416) patients who were subjected to operation, there were 77 patients who had recurrent or persistent carcinoma for about six months following, in most instances, one or more courses of radiation therapy, and, in a few instances, recurrence after radiation and surgery, or after surgery alone (5 cases). *In all of these patients the excised specimens showed viable cancer. No patient was included in this group when the pathological study of the specimens showed only inflammatory changes.* To be sure, operations were performed on some patients who on pelvic examination were thought to have recurrences but where the routine pathologic study of the specimen showed only inflammation. These cases were excluded from this study.

The 77 patients were operated upon, receiving the operation judged appropriate for them[1] and consisting of one of the following procedures: classical Wertheim (1 case), radical hysterectomy and pelvic node excision, anterior pelvic exenteration, or total pelvic exenteration. Age, obesity, cardiovascular disease, diabetes, etc., were not considered contraindications to operation. The extent of the recurrences is evident by the fact that among the 77 patients 40, or 52 per cent, of the operations were either total or anterior pelvic exenterations. Thus the patients in this series as a group were in an appreciably further advanced stage than the 216 recurrent cases cited by Truelsen which were selected for re-radiation because of the small size of the recurrence. Obviously none of the latter had rectal and bladder invasion.

The results achieved in this series of patients are summarized in Table I. It is noted that 42 patients, or 55 per cent of the series, presented invasion of

bladder and/or rectum and/or ureters. Two of these patients did not have exenterations but hysterectomies and node excision with segments of bladder also removed. If this group is excluded there remain 35 patients in whom the disease had not spread to adjacent viscera but sometimes had metastasized to pelvic nodes, and, of these, 16, or 46 per cent of the 35 patients, have survived three and one-half to six years and remain well.

Among the 42 patients who had bladder and/or rectal, and/or ureteral invasion, 8, or 19 per cent of the 42 patients, have remained well three and one-half to six years. Six of these had exenterations. Indeed, only one of this group was operated upon three and one-half years ago, the remainder over four years. One patient who had an anterior partial and four who had total extenerations are living and well over four and one-half to five years after operation. As mentioned previously, in two instances the bladder was invaded but a segmental resection of bladder with radical hysterectomy and node excision only was performed, the patients both surviving over five years. The over-all salvage rate for survival three and one-half to six years free from disease is 24 patients from among 77, or 31 per cent.

The immediate number of deaths from surgery was 9, or 12 per cent of 77 patients. Each of these deaths followed anterior or total pelvic exenteration and one death was among those who had a less radical procedure. This patient succumbed on the thirty-first day after operation of massive hemorrhage from large sloughing pelvic vessels. She had been treated by radiation some months prior to the operation.

TABLE I. RESULTS OF SURGICAL TREATMENT OF RECURRENT CARCINOMA OF THE CERVIX

STAGE OF DISEASE (SURG. & PATH. CLASSIF.[2]). EXTENT OF DISEASE VERIFIED BY HISTOLOGICAL EXAMINATION IN ALL INSTANCES.		LIVING AND WELL	DEAD
Class A. Disease Limited to Cervix.—			
RA	Recurrent after radiation	8	6
SRA	Recurrent after radiation and surgery	3	0
Class B. Invasion of Vaginal Fornices and/or Lower Corpus.—			
RB	Recurrent after radiation	3	5
Class C. Invasion of One or Both Parametria and/or Metastases to Parametrial Nodes.—			
RC	Recurrent after radiation	0	6
SC	Recurrent after surgery	0	1
SRC	Recurrent after surgery and radiation	1	0
Class D. Metastases to Obturator, and/or External Iliac, and/or Hypogastric Nodes.—			
RD	Recurrent after radiation	1	0
SRD	Recurrent after surgery and radiation	0	1
Class E. Cancer Has Invaded Bladder and/or Rectum, and/or Ureters.—			
RE	Recurrent after radiation	6	27
SE	Recurrent after surgery	1	2
SRE	Recurrent after surgery and radiation	1	5
Total		24	53
Survivors 3½ to 6 yrs. = 24/77 = 31% of series.			

In recent discussions concerning the advisability of radical surgery for advanced cancer it has been pointed out that some patients will survive for pro-

longed periods without any form of treatment. While this undoubtedly is true in the exceptional case, it can hardly be expected that all of the 77 patients in this series would have survived for periods of three and one-half or more years without treatment and certainly at the end of a period of three and one-half years, 24, or 31 per cent, would not have presented themselves free from cancer without treatment, i.e., with spontaneous regression. The fact that 42 patients (excluding the 9 surgical deaths and 2 patients who died without evidence of cancer over three years after operation but nevertheless were counted as cancer deaths) died of recurrences within three and one-half years following operation is evidence that the form of cancer dealt with here is not a very slowly progressing one.

Attention is again drawn to the studies of recurrences of after radiation or radiation failure by Truelsen[3] in which among 706 such patients 1.7 per cent were alive after the third year following detection of the recurrences. (The survivors were patients who had small localized recurrences and were re-radiated.) In the series reported here, the average survival rate of those who died of recurrences following operations other than exenteration was 18 months, with extremes of 2 and 49 months. Of those who received an anterior or total exenteration and died of recurrences, the average survival was 11 months, with extremes of 1½ to 54 months; the patient who survived total exenteration for 54 months did not die of cancer but died of extraneous causes; nevertheless this case is counted as a "cancer death."

Summary

1. An unselected series of 77 patients with recurrent cancer of the cervix, in most instances following radiation therapy, is presented. An appropriate radical operation, either radical hysterectomy and pelvic nodes excision or some type of pelvic exenteration, was performed in each instance.

2. The immediate surgical deaths which occurred in the series were one following modified radical hysterectomy and pelvic node excision, and 8 following either anterior or total pelvic exenteration (12 per cent mortality rate for the series). Twenty-four patients are living and well three and one-half to six years after operation. Twenty-one of the twenty-four survivors were operated upon four to six years previously.

3. In this series the patient with cancer of the cervix recurrent after a previous attempt to cure by radiation or relatively conservative surgery was offered another chance for control of the disease by *radical* surgery. The risk of immediate surgical death (death within 30 days of operation) if an exenteration was necessary being 12 per cent. The chances that exenteration would be deemed necessary were 52 per cent in this series. Among those patients in whom an exenteration was not deemed necessary, 32 patients, there are 18 survivors for three and one-half to six years, an incidence of 52 per cent (of 32 patients).

4. Patients with cancer of the cervix treated by radiation should be carefully followed and at the earliest evidence of recurrence in the pelvis should be considered as candidates for the appropriate type of operation in

order to afford them another opportunity for control of the disease, provided that there is no evidence of extrapelvic metastases. If bladder or rectum is not involved, procedures short of partial or total exenteration still have something to offer these patients without the necessity of exenteration. The latter operation, although radical in scope, also offers the opportunity for prolonged survival since "five-year cures" have been achieved.

Addendum.—In addition to the 77 cases described there were 16 patients in whom there had been a histologic diagnosis of carcinoma of the cervix and who were treated by radiation elsewhere. Subsequently they were not well, and, in addition to pelvic pain and often fever, they presented ulcerations in the vault of the vagina, fistulas, indurations of varying degree in the adnexal regions, even to the extent of exhibiting a so-called "frozen pelvis." The clinical picture was that of recurrence and operation was performed. Routine pathologic study failed to reveal viable carcinoma in the specimen but since carcinoma had been present recurrence could not be absolutely ruled out. If these patients were to be included in the foregoing statistics, the salvage rate would be 36 of 93 patients (12 of them surviving over 4 years), or 38 per cent of the series instead of 31 per cent. However, because histological proof of recurrent cancer was not possible, these 16 patients are not included.

References

1. Brunschwig, A.: Am. J. Obst. & Gynec. 61: 1193, 1951.
2. Meigs, J. V., and Brunschwig, A.: Am. J. Obst. & Gynec. 64: 413, 1952.
3. Truelsen, F.: Cancer of the Cervix, Clinical Features With Particular Reference to the Results of Radiotherapy, Copenhagen, Rosenkilde and Bagger; London, 1949, H. K. Lewis & Co., Ltd.

A CELLULAR STUDY OF UTERINE ASPIRATIONS

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THIS is a morphological study of the cellular elements seen in aspirations of the uterine cavity. The work was undertaken in order (1) to determine whether cells from adenocarcinoma could be readily identified in such specimens and (2) to compare the studies of endometrial and endocervical aspirations in the presence of adenocarcinoma of the uterine corpus or fundus.

Materials and Methods

A total of 513 patients undergoing some operative procedure in the Department of Gynecology of the University Hospitals of Cleveland were examined by means of aspirations obtained from the uterine cavity. Specimens were also obtained by aspirating the cervical canal and scraping the ectocervix. Cellular specimens were first obtained from the cervix after which aspiration of the uterine cavity was done. Identified only by number, the specimens were studied objectively so that the results might be compared with those found on histopathological examination.

Aspiration of the uterine cavity was done by one of several gynecologists using a small blunt-tipped laryngeal cannula attached to a syringe. Suction was applied in order to collect specimens from several respresentative sites. The aspirated material was expressed onto the surface of a glass slide and distributed as evenly as possible. The slides were then immersed in a fixing solution composed of equal parts of 95 per cent ethyl alcohol and ether. The method used in obtaining cervical specimens has been previously described.[1] The staining method employed was that described by Papanicolaou.[2] Both the EA 36 and the EA 50† modifications were employed.

Histopathological study of the endometrium was carried out in 395, or 77 per cent, of the 513 patients subjected to endometrial aspiration. There was evidence of localized or diffuse overgrowth of the tissue in 75, or 14.6 per cent, of the cases. This group included 20 patients with proved adenocarcinoma, 15 with cystic hyperplasia, 4 with a more advanced hyperplasia regarded as "atypical hyperplasia," and 36 with polyps. An additional 320 patients showed the following endometrial changes: normal proliferative phase 187, normal secretory phase 60, atrophy 13, nonspecific inflammation 20, lesions associated with pregnancy 17, and 23 instances in which the tissue was considered inadequate for detailed study. In addition to the previously mentioned endometrial changes, 6 patients in this group had invasive cancer of the cervix, 9 had carcinoma in situ, and 31 had dysplasia of the cervical squamous epithelium.

In 118, or 23 per cent, of the 513 patients the surgical procedure performed did not entail the removal of endometrial tissue so that the results could not be verified by histopathological examination. None of the patients in this group showed cellular evidence of adenocarcinoma in the aspirated specimens.

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†Ortho Pharmaceutical Co., Raritan, N. J.

Results

The 513 aspirations of the uterine cavity included 20 taken in the presence of proved adenocarcinoma of the endometrium. In 18 of the specimens there were cells recognized as being from adenocarcinoma. In one case the slides failed to show any cells of endometrial origin due to inadequate sampling. In another case in which the specimen was adequate in amount an interpretation of adenocarcinoma was not possible.

There were 15 aspirations obtained in the presence of cystic hyperplasia none of which were misinterpreted as adenocarcinoma; no attempt was made, however, to identify them specifically as being from hyperplasia of the endometrium. In 3 of the 4 patients who showed an atypical hyperplasia of the endometrium no erroneous interpretation was made. In one case, however, the specimen was regarded as being from adenocarcinoma. The cervical aspiration was also classified as showing cells from adenocarcinoma although it was read independently without knowledge of the results on endometrial aspiration. The histopathological studies indicated an atypical hyperplasia. The aspirations obtained in the presence of polyps were not confused with adenocarcinoma.

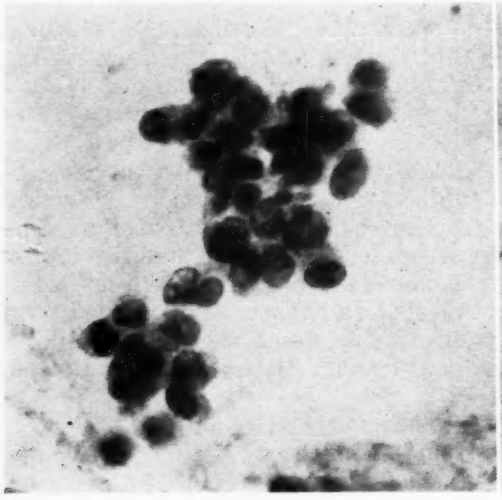

Fig. 1.

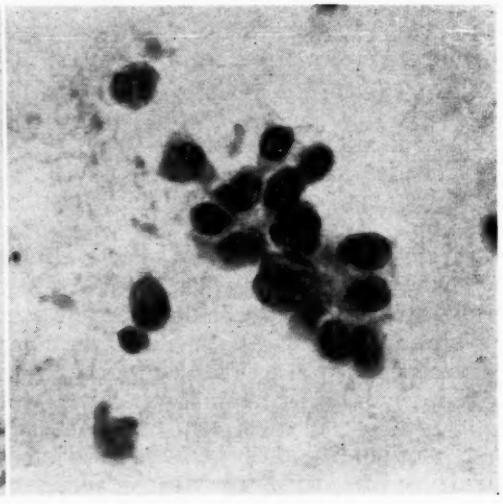

Fig. 2.

Fig. 1.—Normal endometrial cells in endometrial aspiration. (×722.)
Fig. 2.—Normal endometrial cells in endometrial aspiration. (×722.)

The specimen obtained from the uterine cavity was commonly contaminated with cells derived from the cervical canal. In many instances cells from either definite or in situ cancer were seen in the endometrial aspiration. Such cells were more abundant in the aspirations and scrapings from the cervix. The remaining 438 specimens showed no cellular evidence of adenocarcinoma although 118 of the patients were not examined by histological means so that the status of the endometrium was unknown.

While 18 of the 20 endometrial aspirations made in the presence of an adenocarcinoma showed characteristic cellular elements, only 14 of 20 aspirations

of the cervical canal were so interpreted. On review, cellular abnormalities were appreciated in several cases although it is doubtful that the magnitude of the change would have permitted an outright interpretation of adenocarcinoma. The specimens were considered adequate in all instances. There was no correlation between the histologic appearance of the adenocarcinoma and the degree of exfoliation of cells into the cervical secretion.

Morphology

The endometrial cells were isolated or arranged in sheets or aggregates. In sheets the arrangement of each component cell was approximately the same in relation to its neighboring elements. The cell forms were small (Figs. 1 and 2) and showed only limited amounts of cytoplasm. This was finely vacuolated in some instances. Round or oval nuclear forms were common, being eccentric in location in many cells. Nuclear masses varied more in size than in shape. The nuclear membrane was frequently accentuated by an underlying deposition of chromatin, the so-called chromatic membrane. The chromatin pattern was uniformly finely granular with a few slightly larger aggregates or chromocenters. A small nucleolus was apparent in most nuclear forms. Mitoses were rare in the cellular masses during the proliferative phase. While there were other variations in cellular structure throughout the cycle, these were of little significance in determining the phase of the endometrium.

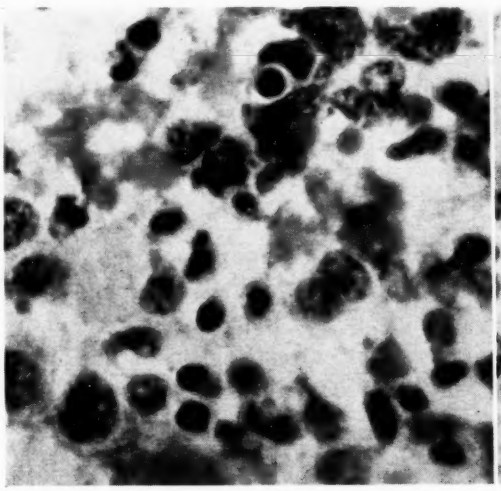

Fig. 3.

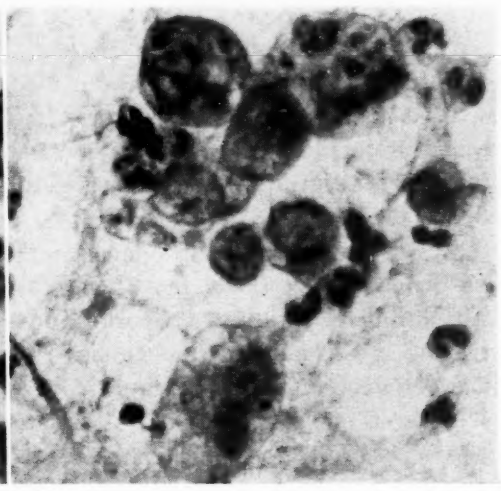

Fig. 4.

Fig. 3.—Malignant tumor cells in endometrial aspiration obtained in presence of less differentiated carcinoma. (×722.)

Fig. 4.—Malignant tumor cells in endometrial aspiration obtained in presence of more differentiated adenocarcinoma. (×722.)

In addition to the epithelial elements in the aspirated material there were also fixed tissue cells apparently derived from endometrial stroma. These resembled histiocytes in that the nucleus was indented and the cytoplasm vacuolated opposite the nuclear indentation. The cells were varied in size and were

identical with free histiocytes observed in cervical secretion. Such cells were usually identified easily and were not confused with endometrial epithelium.

As compared with the malignant tumor cells observed in cervical and vaginal secretions, the cells derived from adenocarcinoma in the endometrial aspiration were more numerous and exhibited less evidence of degeneration. The elements were isolated and arranged in irregular masses. In the latter the cells were irregularly arranged in relation to adjacent cells. In general the forms were larger than those of the normal cells and varied considerably in size and shape depending on the lesion encountered. The cellular borders were indistinct in some cells and well defined in other instances. The cytoplasm was variable in amount and frequently replaced by large vacuoles. Such cells showed phagocytosis in many instances. The nuclear masses were relatively large in relation to the cytosome and were eccentric in location. There was variation in nuclear size and shape. This was most marked in instances where the neoplasm was less differentiated. The nuclear membrane was accentuated and the nuclear chromatin granular. In some forms the masses of chromatin were larger and more discrete so that the space occupied by the nuclear sap was more prominent. In other forms the chromatin was more finely granular and uniform. Chromocenters and nucleoli were noted. Nuclear karyorrhexis, chromatolysis, and pyknosis were apparent in many instances. Mitoses were noted in cellular masses but were not observed in isolated cell forms. Examples of the cellular changes are shown in Figs. 3 and 4.

Comment

Since the appearance of the monograph by Papanicolaou and Traut,[3] there have been numerous published reports dealing with the accuracy of the cellular technique in the presence of uterine cancer. While the reported accuracy shows considerable variation, there is general agreement that adenocarcinoma of the corpus or fundus is more difficult to detect by cellular means. While earlier studies were based on specimens obtained from the vaginal pool, later work has demonstrated the value of aspirations made in other sites. Papanicolaou and Marchetti[4] credit Dr. George Bourgeois and Dr. William Carey for demonstrating the practicality of endometrial or endocervical aspiration in the detection of cancer. The technique involved has been described by Carey.[5] Such methods do not rely solely on the spontaneous exfoliation of the malignant tumor cells but serve to remove them by physical means as well. In general such specimens contain more malignant tumor cells from an accessible tumor as compared with those depending entirely on spontaneous exfoliation.

The large number of failures in the cellular detection of uterine adenocarcinoma are attributed to (1) the degeneration of the exfoliated cells by the time they reach the cervix or posterior vaginal fornix, (2) the sparsity of the cellular elements, (3) associated cervical stenosis in some instances, and (4) a greater difficulty in appreciating changes in smaller cell forms. Of these, cellular degeneration and the sparsity of the cellular elements are probably most important. When aspiration of the endometrial cavity is used, both of these disadvantages

are eliminated or minimized. In addition, the cervical stenosis can also be eliminated as a factor although this may also be eliminated by probing the canal before obtaining cervical aspiration.

Examination of the specimens obtained by aspirating the uterine cavity was more successful in detecting adenocarcinoma than was the study of the cervical secretion. Similar observations were made by Hecht[6] who identified adenocarcinoma correctly in 16 cases while the cervical or vaginal specimen permitted recognition in only 10 of the 16 cases.

It should be emphasized that the present study was not made in order to promote the widespread use of endometrial aspiration in the cellular detection of cancer. The work was carried out only as an experimental procedure. Only competent operators were permitted to take the specimens in order to prevent perforations of the uterus. At the present time the woman with postmenopausal bleeding can be studied to better advantage by curettage and histopathological examination. Such a patient is not a candidate for cellular studies of endometrial aspiration.

Conclusions

1. Among 513 women subjected to endometrial aspirations there were 20 with proved adenocarcinoma. Cellular examination of the endometrial aspiration permitted recognition in 18 of the 20 cases.

2. Cellular studies of aspirated material from the cervical canal revealed recognizable malignant tumor cells in only 14 of the 20 cases with proved adenocarcinoma.

References

1. Reagan, J. W., Seidemann, I. L., and Saracusa, Y.: Cancer **6**: 224, 1953.
2. Papanicolaou, G. N.: Science **95**: 438, 1942.
3. Papanicolaou, G. N., and Traut, H. F.: Diagnosis of Uterine Cancer by the Vaginal Smear, New York, 1943, Commonwealth Fund.
4. Papanicolaou, G. N., and Marchetti, A. A.: Am. J. Obst. & Gynec. **46**: 421, 1943.
5. Carey, Wm. H.: Am. J. Obst. & Gynec. **46**: 422, 1943.
6. Hecht, E. L.: New York J. Med. **52**: 2745, 1952.

AN ANALYSIS OF ONE HUNDRED CULDOSCOPIES

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SINCE 1943 when Decker devised a new culdoscope and described a technique for its use, the instrument has been employed fairly extensively throughout the country. There is considerable disagreement, however, as to its value as a diagnostic gynecological instrument, and because of this it was thought that a critical review of experiences with it in the Sloane Hospital for Women would be of value. We sought an answer to the following questions:

Does culdoscopy improve clinical diagnosis in a sufficient number of cases to justify its use?

Are there instances where its use can be substituted for exploratory laparotomy?

Does culdoscopy give more information than simple posterior colpotomy and not exceed the dangers of the latter?

What, if any, are the technical difficulties of culdoscopy?

What minor or major complications, if any, can be expected to occur following culdoscopy?

Material

An analysis of the first 100 culdoscopies done at the Sloane Hospital since 1947 has been made. These have been divided into three groups: (1) sterility problems, (2) endocrine problems, (3) general gynecological problems.

Cases belonging to more than *one* of the three groups were classified according to the main disorder, i.e., a sterility problem showing occasional anovulation was classified as a sterility problem; a sterility problem with primary amenorrhea was considered as belonging to the endocrine group.

Technique

Although some gynecologists (Palmer, Abarbanel) recommend culdoscopy as an office procedure, all our patients were admitted to the hospital for culdoscopy. The greater number were done under caudal anesthesia.

The patients were prepared according to routine hospital preoperative procedure, and the knee-chest position was used as proposed by Decker. This position gives excellent exposure of the pelvic contents and is not uncomfortable for the patient.

Culdoscopy as Part of a Sterility Investigation.—Culdoscopy was performed on 30 patients who complained of infertility. For the most part, these

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30 patients fell into a group in whom no abnormality could be found after a complete and thorough investigation of both the husband and wife. It was thought that in some of these patients, especially the ones who had a history of previous surgery or infection, there might be pelvic lesions which were not identifiable by tubal insufflation or salpinogogram. A supposition was made, for instance, that even though the tubes opened into the peritoneal cavity, a number of pelvic peritoneal adhesions might separate the ovary from the fimbriated extremity of the tube and thus act as a barrier to progress of the ovum. Several other members of this group had somewhat abnormal findings on pelvic examination such as tender or enlarged ovaries or irregularities in the uterus. One culdoscopy was done to determine the status of a patient who had formerly had an Estes operation since it was thought that the transplanted ovary had become cystic. In 11 patients the peritoneum was not entered and the procedure was discontinued; in the remaining 19 the findings are listed as follows:

NO. OF CASES	FINDINGS
9	Normal pelvic organs
4	Polycystic ovaries
3	Periovarian adhesions
1	Normal-appearing but closed tubes
1	Status post Estes operation
1	Enlarged right cystic ovary and cornual intramural fibroid
19	

Patency of the tubes was tested in 4 patients with methylene blue during the procedure, with tubal closure identified in one case. Periovarian adhesions, observed in 3 patients, were considered sufficient to interfere with the transportation of the ovum from the follicle to the fimbriated end of the tube and were thus thought to be an important factor in the problem of infertility.

A diagnosis of a Stein-Leventhal type of polycystic ovary was made in 4 patients. Considering the high incidence of cure rate of this syndrome following wedge resection of the ovary, a correct preoperative diagnosis was of considerable help since the syndrome was not necessarily suspected.

Culdoscopy as a Part of an Endocrine Investigation.—In cases of otherwise unexplained primary or secondary amenorrhea and menorrhagia, where the etiology of these symptoms is thought to be one of hormonal abnormality, we have heretofore had as diagnostic facilities the benefits of the hormone laboratory. Gonadotrophin and steroid hormone assays are difficult, space consuming, and expensive, and sometimes difficult to interpret. Actual visualization of the ovaries has been found to be of great value as a diagnostic aid especially in cases of amenorrhea. Therefore, culdoscopy has now become almost a routine procedure in those cases where a disorientation of hormonal activity is suspected. A simple case report may effectively indicate the value of this procedure.

E. H., aged 24 years and married for four years, was first seen with a chief complaint of amenorrhea and sterility. The patient had never menstruated spontaneously and from the age of 16 had been given extensive hormone therapy of all types and varieties over

long periods of time. Various types of hormone therapy had resulted in episodes of vaginal bleeding. The patient had otherwise been healthy with no operations or severe illnesses. She married four years ago, never used contraceptives, and had satisfactory sexual relations and normal libido. Physical examination disclosed an apparently normal woman of 24 years. Pubic and axillary hair were present but somewhat less than normal, and breast development was definite but also somewhat less than normal. Pelvic examination disclosed normal external genitals and a normal vagina with normal vaginal mucous membrane. There was a small nulliparous cervix, and a small uterus about twice the size of an adult thumb could be felt in normal position and with normal motility. No masses or tenderness were felt in the adnexal region. Vaginal smear disclosed two plus estrogen activity.

With a situation thus presented where lack of normal ovarian activity was certainly apparent, a culdoscopy was decided upon. This procedure disclosed complete absence of any ovarian tissue in the normal site for ovarian growth. On the posterior surface of the broad ligaments on both sides, the uteroovarian ligament could be made out, at the lateral extremities of which was a white ligamentous structure about 2 cm. long by 1 or 2 mm. in diameter. This was thought to be the mesovarium.

This case was considered to be one of complete ovarian agenesis unless it could be assumed that some ectopic focus of ovarian tissue was present. A more likely source of her slight estrogenic activity, however, was thought to be the adrenal gland, especially when a later gonadotrophin assay disclosed a menopausal level of excretion.

The positive diagnosis thus made not only revealed the uselessness of past or future hormonal therapy in an effort to produce ovarian stimulation, but also made it possible to clarify in the patient's mind her exact status concerning the problem of sterility, and thus enable her to be definite about her future.

It has been of great value to identify not only the absence of ovarian tissue but the presence of abnormal ovarian tissue in cases of menstrual abnormalities as has been previously mentioned. The identification of the so-called Stein-Leventhal ovary is easily possible by means of culdoscopy and provides a definite conclusion concerning future types of therapy.

In our series, culdoscopy was attempted 19 times for various menstrual disturbances. In 5 instances the peritoneal cavity was not entered. The remaining 14 are listed as follows:

NO. OF CASES	FINDINGS
6	Polycystic ovaries
4	Ovarian agenesis
1	Small hydatid cyst (which was thought to be a granulosa tumor)
1	Simple ovarian cyst
1	Chronic inflammatory changes of tubes and ovaries
1	Normal pelvic organs
14	

Culdoscopy in General Gynecological Differential Diagnosis.—Pelvic pain and menstrual abnormalities accompanied by equivocal pelvic findings frequently offer a large variety of differential diagnoses to the gynecologist. Although history, physical findings, and some laboratory procedures may suggest certain possibilities, occasionally it is only by actual visualization of the pelvis that a definite diagnosis can be made. This necessitates either exploratory laparotomy or culdoscopy.

Fifty-one culdoscopies were carried out on patients who fell into this category. In 36 the peritoneal cavity was adequately visualized. The difficulty of a correct diagnosis in suspected extrauterine pregnancies is well documented by our figures. The possibility of ectopic pregnancy had to be taken into consideration in 28 cases. This was confirmed in only 9 cases, while the other 19 were found to be other gynecological diseases of various types not necessitating laparotomy. Thus laparotomy was avoided in a large number of cases.

It might be interesting at this point to compare the relative values of culdoscopy to simple needle puncture of the cul-de-sac as useful procedures in attempting to establish the differential diagnosis of ectopic pregnancy. Needle puncture of the cul-de-sac is obviously a more simple procedure than culdoscopy, but it must be remembered that its only usefulness is to establish whether or not there is blood present in the pouch of Douglas. Either the presence or absence of blood may result in an erroneous conclusion. An ectopic pregnancy may be unruptured and therefore, not bleeding, whereas, on the other hand, bleeding may very well come from a ruptured follicle or a bleeding corpus luteum cyst. This actually was the case in 4 instances in our series in which culdoscopy was done.

The increased percentage possibility of diagnosing unruptured ectopic pregnancy by means of the culdoscope may possibly be of considerable value aside from the obvious usefulness in preventing hemorrhage. Immediate laparotomy following diagnosis may enable the surgeon to remove the unruptured ectopic pregnancy from the tube, leaving the tube relatively intact.

Three times endometriosis was suspected, but in none of these cases could the diagnosis be confirmed. Our only case of endometriosis was not suspected preoperatively. The findings of this group are as follows:

NO. OF CASES	FINDINGS
14	Unsuccessful
3	Nonmalignant ovarian cysts
19	Suspected but not confirmed ectopic pregnancies (adhesions, fibroids, intrauterine pregnancies, etc.)
9	Confirmed ectopic pregnancies
1	Endometriosis
5	Salpingitis and adhesions
51	

Technical Difficulties.—In 30 out of 100 cases, the pelvic organs could not be seen. This high incidence of failure most frequently occurred in 1947 and 1948 during the early use of the culdoscope in our clinic. Further experience greatly improved the technique, and it is now only rarely that the peritoneal cavity is not entered. It may be noted that it is extremely important to push the cervix forward toward and under the symphysis rather than to draw it toward the introitus. The posterior fornix is then well exposed and sufficient tension is present in the vaginal mucous membrane and the peritoneal reflection of the pouch of Douglas in opposition to it. The trocar may then be efficiently thrust into the abdominal cavity. Obesity and thick layers of

retroperitoneal fat occasionally make the puncture difficult, and this was thought to be a contributing factor in 4 failures. Adhesions and chronic pelvic inflammatory disease complicate successful culdoscopy; in our experience, this was thought to be the case in 13 instances. There are 9 cases in which no obvious reasons could be found to explain the failure of the procedure.

Complications.—There was one major complication in our series, a report of which follows:

Mrs. G. A., No. 602194, was a 30-year-old housewife with a chief complaint at admission of menometrorrhagia. Previous dilatation and curettage had been negative. A tentative diagnosis of the pelvic congestion syndrome with chronic parametritis was made, and a culdoscopy was performed in order to rule out endometriosis. Under local anesthesia, the posterior fornix was easily perforated and the pelvic organs visualized. Many adhesions and a right salpingitis were described at that time. Following the procedure, she complained of severe shoulder pain during the first two days. She was discharged on the fourth day following the procedure. It was learned one month after discharge, that on the seventh day following culdoscopy, she had suffered a severe vaginal hemorrhage. She was admitted to another hospital, blood transfusion was given, and the vagina packed. The next day the packing was removed, and the culdoscopy wound was found gaping. A curettage was then performed, and the opening in the posterior cul-de-sac was closed with four sutures. Further follow-up was uneventful as far as the culdoscopy was concerned.

Minor complications consist of frequent shoulder pain due to the accumulation of air under the diaphragm. It has been prevented to a certain extent by expressing as much air as possible following the procedure. There was no evidence of infection in this series nor any trauma to the intestine.

Conclusions

The 70 cases in which culdoscopy was successful have been divided into four groups:

1. Cases in which only laparotomy or culdoscopy could have established a correct diagnosis and laparotomy was avoided through the information obtained at the time of culdoscopy (28 cases).

2. Cases in which only laparotomy or culdoscopy could have established the correct diagnosis, laparotomy being indicated by the diagnosis made at the time of culdoscopy (26 cases).

3. Cases in which inspection by culdoscopy had given useful information concerning diagnosis or prognosis which otherwise could have been obtained only by laparotomy (15 cases).

4. Cases in which culdoscopy gave no contribution to the diagnosis or prognosis and could have been avoided (1 case).

We thus assume that culdoscopy was of value as a diagnostic procedure in at least 43 of 70 cases in that it established a diagnosis and at the same time saved the patient the necessity of a laparotomy. In 26 more cases it provided valuable diagnostic aid in deciding whether or not a laparotomy was necessary.

USE OF MODIFIED INSUFFLATION CANNULA FOR SUCTION ENDOMETRIAL BIOPSY IMMEDIATELY FOLLOWING UTEROTUBAL INSUFFLATION AND HYSTEROGRAPHY

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THE idea of diagnosing the endometrial status from small fragments of endometrium was first rejected by eminent pathologists. The senior author (I. C. R.), having observed small nests of endometrium in the fenestra of the uterine cannula used in uterotubal insufflation, thought they might serve the purpose of checking the functional status of the endometrium at the same time that tubal patency was determined.[1] When sections of these small endometrial fragments were shown to Robert Meyer, in 1930, he expressed the opinion that they were inadequate for the diagnosis of the endometrial status. He stated that the endometrium was not uniformly affected throughout its structure and, unless all of it were curetted, a correct mirror of the hormonal effects would not be obtained. Further work, therefore, along this line was abandoned for the time being.

S. S. Rosenfeld[2] is the first investigator who combined suction biopsy with uterotubal insufflation. His paper on "Simultaneous Performance of Rubin Test and Endometrial Biopsy" was published in 1944 and was based on 22 cases. Rosenfeld discontinued the procedure* because he obtained "a few unsatisfactory specimens with the perforated cannula." He subsequently resumed the method, "using the Rubin cannula without side perforations, followed by a curettage employing an endometrial biopsy curet." Increasing experience with endometrial aspiration biopsy, aided by excellent canalized curettes, such as those designed by Klinger and Burch,[3] Novak,[4] Randall,[5] Meigs,[6] and others, has shown that considerable information can be obtained with regard to the relation between uterine and ovarian function by the histological examination of small mucosal fragments. Its value now is generally accepted. This is largely due to the work of E. Novak who pioneered in the use of the suction curette and has repeatedly urged its adoption for endometrial biopsy as a semiambulatory method of distinct advantage to the patient.

Uterotubal insufflation and hysterography are nonsurgical procedures which as a rule are employed in office practice. When followed by aspiration through the same insufflation cannula, endometrial fragments of a size suit-

*Personal communication, March 2, 1953.

able for biopsy purposes are obtainable. The aspiration is unattended by any severe degree of pain or discomfort. To obtain larger fragments than is possible through the small holes of the uterine cannula ordinarily used for insufflation or hysterography, the apertures were widened, measuring 2 by 3 mm. at the tip and 4 by 2 mm. at the sides. Aspiration with the modified cannula tip has proved in our hands a convenient method of adding significant data to the investigation of a sterility problem or of checking the presence of a suspected cancer, thus saving the patient time and inconvenience entailed by extra office visits for these special procedures. It is understood that suction biopsy always follows the other procedures in order to prevent intravasation and embolization.[2, 7] The possibility of the occurrence of the latter mentioned accidents is minimal when the insufflation cannula is used. With the use of the suction curette or curettage, deeper and wider denudation occurs, opening up more vascular portals of entry of the conrast fluid. But this danger is avoided by taking the suction biopsy as the last step in the procedure.

Method

After uterotubal insufflation or hysterography, a 20 c.c. syringe is attached to the outer end of the cannula. With the cannula maintained firmly within the uterus, the plunger of the syringe is withdrawn, generally to the 15 or 20 c.c. mark. While this negative pressure is kept, the cannula is slowly withdrawn. A small amount of endometrial tissue tinged with blood is thus aspirated into the syringe. The syringe is detached from the cannula and the contents expelled into a specimen jar containing neutralized 10 per cent formalin solution. The syringe is then filled with formalin solution and the cannula is flushed out into the specimen jar. The cannula can be flushed out a sufficient number of times to dislodge thoroughly all fragments of tissue. In exceptional cases, where little material is obtained, the aspiration can be repeated without causing appreciable discomfort. Solutions other than formalin, or some other chosen fixative, should not be used for flushing the cannula. In two instances, water or oxycyanide solution was used and produced artifacts by hydration of

TABLE I. HISTOLOGICAL FINDINGS IN 98 CASES

Endometrial polyp		5
Proliferative endometrium		13
With chronic endometritis	1	
With adenomatous hyperplasia and endometrial polyp	1	
Interval endometrium		29
With endometrial polyp	3	
With chronic endometritis, endometrial polyp, and Cervical polyp	1	
With cervical polyp	1	
Secretory endometrium		30
With endometrial polyp	3	
With adenomatous hyperplasia	1	
Nonfunctioning endometrium		6
With endometrial polyp	3	
Mixed phase endometrium with adenomatous hyperplasia		1
Hyperplasia of endometrium		1
Atrophy of endometrium		1
Chronic endometritis		1
Carcinoma of endometrium		2
Quantity not sufficient		9
Total		98

the tissue. If suction is to be repeated, another sterile cannula, if available, may be used, or the one flushed with formalin should be resterilized before insertion into the uterine cavity.

Observations

A series of 100 consecutive cases was examined by the method previously outlined after 60 uterotubal insufflations and 40 hysterographies.* Two specimens were spoiled. The results are summarized in Table I.

In 6 cases, a suction biopsy was obtained immediately before a diagnostic curettage. The diagnosis was made on each preparation independently and the results compared. In 2 cases, the aspirated endometrial fragments were flushed from the cannula with water or oxycyanide solution, prior to fixation in formalin. The aspirated material was hydrated and the cells simulated a secretory phase (Fig. 1, left). The curettings, which were in formalin, revealed a proliferative endometrium (Fig. 1, right). In the other 4 cases, in which formalin was used to flush the cannula, the histological picture of the aspirated material was similar to that of the curettings. (Figs. 2, 3, 4, 5, and 6 represent different phases of the endometrium.)

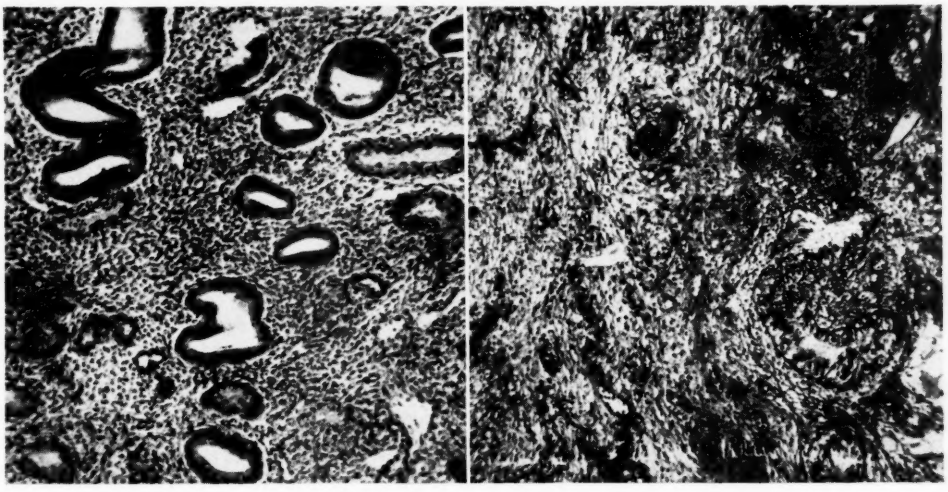

Fig. 1.—Comparison of aspiration biopsy and endometrium obtained by curettage to illustrate the result of incorrect preparation of tissue. The tissue obtained by curettage (left) was fixed immediately in 10 per cent neutralized formalin. The aspirated material (right) was first washed out of the curette with saline or water and then fixed in formalin. The tissue became hydrated and distorted, producing results easily leading to error in diagnosis. Compare with subsequent photos from preparations in which tissues were washed from the curette with formalin solution. (×90, reduced ⅕.)

The percentage of failure to obtain sufficient tissue for study was compared with the percentage in two control series of 100 cases each. The first series consisted of 100 diagnostic curettages, exclusive of cases of pregnancy, performed in the hospital. The second series consisted of 100 biopsies obtained in office practice by the use of an endometrial biopsy curette. In each group, insufficient material was obtained in 6 per cent. In the present series,

*Polyvinyl pyrrolidone with sodium acetrizoate (Salpix), prepared by Ortho Pharmaceutical Corporation, was used for hysterography.

Fig. 4.

Fig. 3.

Fig. 2.

Fig. 2.—Late proliferative endometrium, patient 30 years of age. (×135, reduced ⅓.)
Fig. 3.—Aspiration biopsy of early secretory endometrium, patient 32 years of age. (×90, reduced ⅓.)
Fig. 4.—Nonfunctioning endometrium and chronic active endometritis, patient aged 49 years. (×200, reduced ⅓.)

A. *B.* *C.*

Fig. 5.—This figure illustrates the amount of material obtainable by aspiration. There was interval endometrium (left), an endometrial polyp (center) and an endocervical polyp with chronic inflammation. Patient aged 44 years. (×90, reduced ⅓.)

6 of the failures occurred among the first 50 and 3 in the last 50 aspirations. As is evident from these findings, the suggested method compares favorably with both hospital and office procedures. With more experience, the percentage of failures undoubtedly can be reduced below our first results.

Two cases of endometrial carcinoma were encountered in the series. The data are presented briefly.

CASE 1.—E. H., a nullipara, aged 44 years, bled off and on for one year, following a two-year period of amenorrhea, during which she considered herself to be in the menopause. Several Papanicolaou smears, done abroad and elsewhere in this city, were reported negative for carcinoma. On physical examination, the uterus was found undeveloped and a small amount of clotted blood was seen to escape from the cervix. A hysterogram was done, immediately followed by suction biopsy. The biopsy showed endometrial carcinoma (Fig. 7), corroborating the hysterographic findings, which were later confirmed by hysterectomy.

CASE 2.—A. S., a para ii, aged 69 years, had received a castrating dose of x-rays at the age of 39 for menometrorrhagia. The menopause set in about three months later. For ten years prior to the time of her examination, she had taken stilbestrol. There had been vaginal bleeding for the last three weeks. The uterus appeared large for her age and corresponded in size to an average normally developed organ. Suction biopsy following hysterography confirmed the diagnosis of endometrial carcinoma demonstrated on the x-ray film. The operative specimen showed the carcinoma to be situated in the right horn.

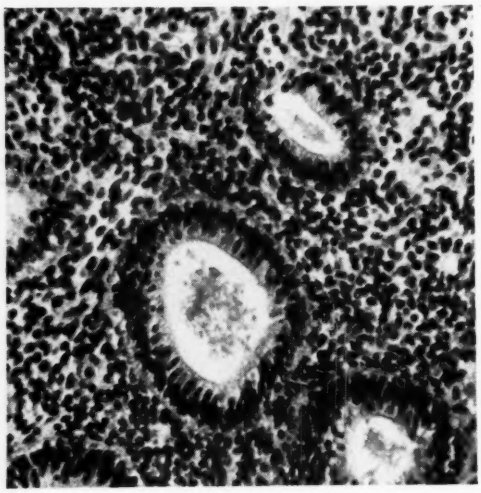

Fig. 6.

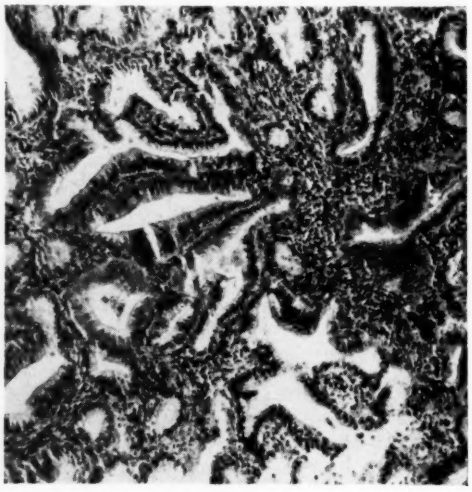

Fig. 7.

Fig. 6.—Hyperplasia of endometrium in patient 68 years of age under self-administered estrogens for a long period. A small superficial carcinoma was subsequently found deep in one horn of the uterus, removed a few weeks later. (×200, reduced ⅕.)

Fig. 7.—Carcinoma of endometrium, patient aged 43 years. (×90, reduced ⅕.)

Summary

Suction biopsy of the endometrium, by means of a modified uterine cannula employed in uterotubal insufflation and hysterography, was carried out in 100 consecutive cases immediately following these diagnostic procedures. Adequate material for histological examination was obtained in 91 per cent of

the series. The method compares favorably with the use of suction curette for obtaining adequate endometrial biopsies and with diagnostic curettage carried out in a hospital. It has the advantage of being a simple, practically painless office procedure by which a sufficient amount of endometrial tissue is obtained for biopsy purposes. Adequacy of the method is shown by the findings of 10 endometrial and 2 cervical polyps among the 100 consecutive biopsies and 2 cases of endometrial carcinoma corroborated by subsequent hysterectomy. If an insufficient amount of tissue is obtained after the first aspiration, it may be repeated once or twice at the same examination without causing undue discomfort to the patient. The economic and timesaving advantages of combining the three diagnostic methods have been stressed.

References

1. Rubin, I. C.: Am. J. Obst. & Gynec. **20**: 28, 1930.
2. Rosenfeld, S. S.: Am. J Surg. **64**: 385, 1944.
3. Klinger, H. H., and Burch, T. C.: J. A. M. A. **99**: 559, 1932.
4. Novak, E.: J. A. M. A. **104**: 1497, 1935.
5. Randall, L. T.: Proc. Staff Meet., Mayo Clin. **11**: 58, 1936.
6. Meigs, J.: Am. J. Obst. & Gynec. **38**: 161, 1939.
7. Rubin, I. C.: J. A. M. A. **15**: 698, 1953.

PROGNOSIS IN CHILDHOOD URINARY TRACT INFECTIONS IN GIRLS*†‡

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In 1937 Wharton, Gray, and Guild[1] published the results of a follow-up of 30 cases of pyelitis in infancy and childhood. In only 13 of these 30 cases was the urinary tract found to be entirely normal. The criticisms of the study, which the authors offered, were, first, that the series was a small one, and, second, that the cases were obviously those representing the most serious infections, since all but 3 of the group had been hospitalized at the time of the initial episode.

In an effort to answer these criticisms of that report, we selected from the files of the Harriet Lane Home all cases in which a diagnosis of urinary tract infection or pyelitis had been made five or more years prior to this study. Efforts were made through letter and social service visits to contact these patients, and to induce them to return for urologic study. The cases were entirely unselected. Any patient who agreed to return, if the original records showed sufficient evidence to substantiate a diagnosis of urinary tract infection, was admitted to the study group. As to the severity of the intial episode, only 18 of the 76 patients required hospitalization, and in several instances coincidental infection elsewhere was the indication for admission.

Of the entire group, only 80 patients could be traced and induced to return for investigation. Four of these, on more thorough inspection, were rejected as having had insufficient evidence of urinary tract infection to be included. In the remaining 76 cases, there were 29 white and 47 negro girls, a ratio similar to that in the group which could not be followed. The ages at the time of initial infection varied 7 months to 13 years, and at the time of the study, from 7 to 32 years. The elapsed period from the time of the primary disease varied from five to twenty-three years.

Preliminary to reporting our results, we must state that, in most instances, there was little demonstrable evidence of upper tract disease with the initial episode and, because of the mild nature of the illness, the urologic data were minimal. Cultures, repeated analyses, nonprotein nitrogen determinations, function and radiographic studies were present in only rare instances. Since one of the aims in this presentation, however, was to study cases with slight as well as those with more severe infections, the clinician's diagnosis with minimal laboratory confirmation was accepted.

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Since the majority of the patients were in excellent health and asymptomatic and engaged in active home, school, or business life, the study could not involve any examination too time consuming or incapacitating. Consequently the features of the follow-up study resolved into interval history, physical examination, urine analysis of catheterized specimen, urine culture on agar slants, nonprotein nitrogen determination, and intravenous pyelography. If any abnormality was discovered in these studies, we attempted to induce the patient to return for further investigation. In spite of many letters and visits, we were successful in only a few instances in completing these studies. The final results, therefore, often left something to be desired, and we present the data with full knowledge of this shortcoming.

In order not to become repetitious concerning certain features of the study which, although recorded, did not differ significantly in the individual groups, we will make several generalizations. The patients were in good health in almost every instance. The condition was described as fair in only 3 instances, and in these the urinary tract was normal in 2 and showed slight ureteropelvic junction obstruction in one instance. Foci of infection, such as dental caries and tonsillar disease, were found not uncommonly, but strangely enough in only one of the 13 patients with recurrent infection and upper tract disease was the focus prominent enough to be noted. Again, in the latter case, disease was minimal and the urine was sterile. Symptoms suggestive of urinary tract disease were present occasionally but these were usually minimal and not annoying enough for the patient to have sought aid except in two cases. Both of the latter occurred in Group IIB, those with more severe disease. In one case, No. 67, this infection was the only abnormality found. In the other case, No. 59, the infection was the most marked of the entire group. This case will be described later. However, for the most part, the occurrence of minimal symptoms such as occasional nocturia or burning was elicted only on direct questioning. Furthermore, there was no correlation between these occasional symptoms and the presence of absence of urologic abnormality.

In grouping the patients, we used only two criteria as evidence of urologic abnormality. The finding of pyuria and positive culture in the follow-up of a case was considered to be significant. However, one or the other alone, as will be noted in the charts, was not accepted as sufficient evidence of urinary tract disease. This, of course, was not true of the initial attack since the majority of the patients had no record of urine culture. Second, pyelographic evidence of abnormality, with or without positive urine findings, was accepted as evidence of disease. Nonprotein nitrogen determinations were unsatisfactory in that the patients were all ambulatory and were not always fasting.

In order to compare our results with those of Wharton, Gray, and Guild we have divided our cases into groups as suggested by those authors. Those groups are:

Group I. Those patients who had had only one attack of urinary tract infection.

Group II. Those patients who had had more than one attack.

Each group was then subdivided into: (A) those patients with no evidence of urologic disease, and (B) those with urologic abnormality. Table I shows comparative figures in the two studies.

TABLE I

	WHARTON, GRAY, AND GUILD		OUR STUDIES	
	CASES	PERCENTAGE	CASES	PERCENTAGE
Group IA	3	33.3	37	68.5
IB	6	66.7	17	31.5
IIA	9	42.9	9	40.9
IIB	12	57.1	13	59.1

TABLE II. GROUP IA

CASE NO.	AGE AT INITIAL ATTACK	ASSOCIATED DISEASE	HOSPITAL ADMISSION	AGE AT PRESENT	URINE WITH INITIAL ATTACK		URINE AT PRESENT		INTRAVENOUS PYELOGRAMS
					WBC	CULTURE	WBC	CULTURE	
18	3	Rhinopharyn.	No	12	++++	-	Occasional	-	Normal
19	-	-	No	12	+	-	Rare	Subtilis	Normal
20	2	-	No	11	20-60/hpf	-	Occasional	Diphtheroids	Normal
21	7	-	No	12	Clumped	-	Rare	Diphtheroids	Normal?
22	8	Gonorrhea	No	13	25-30/hpf	*B. coli*	0		Normal?
23	4	Pneumonia	Yes	11	8-10/hpf	-	-	-	Normal
24	3	Tonsillitis	No	8	++++	-	0	-	Normal
25	2½	Tonsillitis	No	22	Clumped	-	0	Sterile	Normal
26	4½	Tonsillitis	No	18	Many	-	0	Sterile	Normal
27	2	Pneumonia	No	20	+++	-	0	Sterile	Normal
28	3	Tbc.	No	8	+++	-	0	Sterile	Normal
29	4	-	No	19	Many	-	0	Sterile	Normal?
30	5	-	Yes	16	+	-	0	Sterile	Normal
31	8	-	No	31	Clumped	-	Rare	-	Normal
32	2½	-	No	14	5-10/hpf	-	1-2/hpf	Sterile	Normal
33	3	-	No	9	12-15/hpf	*Staph.*	0	Sterile	Normal
34	1¼	-	No	19	++++	-	1-3/hpf	Sterile	Normal
35	10	-	No	15	30-40/hpf	Sterile	0	Sterile	Normal
36	5	-	No	20	Clumped	-	-	-	Normal
37	-	-	-	22	+	-	0	-	Normal
38	5	-	No	21	Clumped	-	0	Sterile	Normal
39	12	Pneumonia	Yes	18	12-15/hpf	-	0	*Staph. albus*	Normal
40	2	-	No	18	Loaded	-	0	*Staph. albus*	Normal
41	4	-	No	9	100 +	-	0	*Staph. albus*	Normal
42	2	-	Yes	11	++++	-	0	*Staph. albus*	Normal
43	1	Tbc.	No	9	Clumped	-	0	*Staph. albus*	Normal
44	8½	-	No	13	35/hpf	-	-	*Staph. albus*	Normal
45	6	Pneumonia	Yes	17	++++	-	-	*Staph. albus*	Normal
46	8	-	No	13	Loaded	*Staph. albus*	0	*Staph. albus*	Normal
47	3	-	No	16	Loaded	-	0	*Staph. albus*	Normal
48	3	-	No	10	10-20/hpf	-	0	*Staph. aureus*	Normal
49	13	-	No	19	10-12/hpf	-	0	*Staph. albus*	Normal
50	4	-	No	24	Clumped	-	0	*Staph. albus*	Normal
51	4½	-	No	16	++++	-	0	*Staph. aureus*	Normal
52	2	-	No	19	Clumped	-	0	*Staph. albus*	Normal
53	3¼	-	No	19	Clumped	-	0	*Staph. albus*	Normal (pregnancy)
54	2¼	Otitis-media	No	16	Many	-	0	*Staph. albus*	Normal

Table II summarizes briefly the findings in Group IA, both at the time of the initial infection and in the present study. Those 37 patients had had only one attack of urinary tract infection and, as is noted in the table, no

urologic abnormality was found at this time. The initial attack was obviously mild in that only 5 of the patients required admission and in 3 of these the indication was a concomitant pneumonia. The interval between the diagnosed infection and the present study varied from five to twenty-three years, and as far as could be determined the patients had had no episode suggestive of urinary tract infection in the interim.

TABLE III. GROUP IB

CASE NO.	AGE AT INITIAL ATTACK	ASSOCIATED DISEASE	HOSPITAL ADMISSION	AGE AT PRESENT	URINE WITH INITIAL ATTACK		URINE AT PRESENT		INTRAVENOUS PYELOGRAMS
					WBC	CULTURE	WBC	CULTURE	
1.	12	—	No	18	++++	—	8-10	*Staph. albus*	Dilatation, ureter and pelvis, rt.
2.	2½	Gonorrhea	Yes	11	10-12	—		*E. coli*	Huge hydronephrosis, rt.
3.	13	—	No	20	20-25	—	0	Sterile	Dilatation, ureter and pelvis, rt.
4.	9	—	Yes	16	Occasional	*B. coli*	0	Diphtheroids	Obstruction ureteropelvic junction, left
5.	7	—	No	14	+++	—	Occasional	Gamma strep.	Slight dilatation, bilateral
6.	6	—	No	14	++	—	0	Sterile	Slight dilatation, left
7.	7 months	—	Yes	20	Clumped	—	-	Gamma strep.	Dilatation, rt. Stricture, bilateral
8.	2	Tonsil	No	11	+++	—	1-3	*Staph. albus*	Stricture, ureteropelvic junction, left
9.	2½	—	No	16	Loaded	—	0	Sterile	Dilatation, ureter and pelvis, right
10.	10	—	No	16	7-8	*B. coli*	0	Sterile	Slight dilatation, right
11.	6	Pharynx	No	11	40-50	—	0	Gamma strep.	Slight dilatation, right
12.	10	Gonorrhea	No	15	+++	—	0	*Staph. albus*	Obstruction, ureteropelvic junction, right
13.	5	Measles	No	9	+++	—	0	Diphtheroids	Slight dilatation, bilateral
14.	2	—	No	8	+++	—	0	*Staph. albus*	Slight dilatation
15.	4½	—	No	25	Clumped	—	3-5	Gamma *Strep. fecalis*	Normal
16.	6½	Pharynx	No	19	Many	—	3-4 with occasional clumping	Hemolytic *Staph. albus*	Normal
17.	1½	Pneumonia	Yes	17	Clumped	—	10-15	*Staph. aureus*	Pregnant, otherwise normal

Group IB consisted of 17 patients who had had only one attack of urinary tract infection but in whom the present study revealed evidence of urologic disease. Table III records the findings in this group. Ages at time of initial episode and interval showed no significant variation from those of Group IA. Again the systemic manifestations were serious enough to demand hospitalization in only 4 of the 17 cases and in at least one case the indication for admission was pneumonia.

Fig. 1.—Retrograde pyelogram in Case 2 showing marked hydronephrosis and normal ureter.

Fig. 2.—Injection of calyces, pelvis, and upper ureter in Case 2 after nephrectomy.

In 3 of the 17 cases, Nos. 15, 16, and 17, pyuria and positive cultures were the only evidence of urologic abnormality, pyelograms being normal. In the remaining 14 cases, only 3 were found to have both pyuria and positive cultures. Pyelographic changes were noted as indicated in Table III.

Pyelography revealed marked hydronephrosis with colon bacillus infection in one case. Ureteropelvic junction obstruction was noted in 3 cases, unilateral dilatation in 7, and bilateral dilatation in 3. In these 13, the urologic abnormality was considered to be minimal. In only one case (Figs. 1 and 2)

was the pathology striking enough to produce severe damage, differential phthalein revealing 5 per cent function on the right as opposed to 20 per cent on the left. In view of the persistent infection and damaged kidney, nephrectomy was performed. An aberrant vessel was found to have produced the pathology in this instance. An example of the minimal type of pathology present in the major portion of the group is seen in Fig. 3.

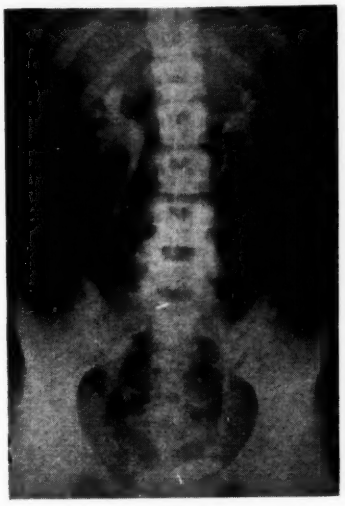

Fig. 3.—Intravenous pyelograms in Case 7, showing minimal dilatation of right urinary tract with narrowing at the uterovesical junction.

The findings in Group IIA, that is, those patients who had had repeated infections but in whom the present study revealed no evidence of urinary tract disease, are given in Table IV. As in the previous groups the initial episode was severe enough to demand hospitalization in 2 instances, although pneumonia was the obvious indication in one of the 2 cases. Six of the 9 patients had had only one recurrence, 2 had had two recurrences, and one, four episodes following the initial attack. The age at the time of the initial infection

TABLE IV. GROUP IIA

CASE NO.	AGE AT INITIAL ATTACK	ASSOCIATED DISEASE	ADMISSION	AGE AT PRESENT	URINE WITH INITIAL ATTACK		URINE AT PRESENT		INTRAVENOUS PYELOGRAMS
					WBC	CULTURE	WBC	CULTURE	
68	2	—	No	22	+++	-	0	Sterile	Rotation, otherwise normal
69	5	Scabies	No	17	+++	-	0	Alpha strep.	Double pelvis, otherwise normal
70	4	—	No	11	2-6/hpf	-	0	Diphtheroids	Normal
71	2	—	Yes	11	Clumped	-	0	Sterile	Normal
72	3	Rickets	No	15	Loaded	-	0	Sterile	Normal
73	2½	—	No	13	Many	-	0	Hemolytic *Staph. albus*	Normal
74	8½	Otitis media	No	21	Clumped	-	0	*Staph. albus*	Normal
75	7	—	No	15	3-5/hpf	-	0	*Staph. albus*	Normal
76	9 months	Pneumonia	Yes	19	Many	-	-	*Staph. albus*	Normal

TABLE V. GROUP IIB

CASE NO.	AGE AT INITIAL ATTACK	ASSOCIATED DISEASE	ADMISSION	AGE AT PRESENT	URINE WITH INITIAL ATTACK		URINE AT PRESENT		INTRAVENOUS PYELOGRAMS
					WBC	CULTURE	WBC	CULTURE	
55	2	—	Yes	22	++++	*B. coli*	5-10	*E. coli*	Hydronephrosis and ureter, rt.
56	3½	—	Yes	15	Loaded	*B. coli*	3-5	*E. coli*	Hydronephrosis and ureter, rt.
57	7 months	—	Yes	7	+++	*B. coli*	Few	*Staph. aureus*	Hydronephrosis and ureter, rt.
58	3	Tonsillitis	Yes	10	12	*B. coli*	—	Diphtheroids	Hydronephrosis, stricture, and ureteropelvic junction obstruction, rt.
59	4½	—	Yes	10½	+++	Flexner bacillus	++++	Flexner	Hugh hydronephrosis, bilateral
60	7	Pneumonia	No	22	Loaded, clumped	*B. coli* (1935)	20-25	*B. coli*	Hydronephrosis, rt.
61	10 months	—	No	14	6/hpf	—	0	Sterile	Hydronephrosis, rt.
62	2	—	No	17	Loaded, clumped	—	25-35	*Staph. albus*	Dilatation, urinary tract, rt.
63	2	—	Yes	9	50/hpf	*B. coli*	+	Lost	Dilatation, urinary tract, rt.
64	4½	—	No	19	5-10/hpf	—	0	*Staph. albus*	Double pelvis and ureter, lt., with dilatation
65	2½	Pneumonia	Yes	18	Clumped	—	0	*Staph. albus*	Hydronephrosis, lt.
66	6	—	Yes	13	+++	*B. coli*	1-3	*Staph. albus*	Normal
67	10	Gonorrhea	No	15	40-50/hpf	—	Loaded	*Staph. albus*	Normal

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and the interval to the present study were not significant. Urine was routinely clear microscopically, and although cultures were positive in 6 instances these were not considered evidences of disease in the absence of pyuria and pyelographic abnormality.

The final group of 13 cases described in Table V were those who had had repeated urinary tract infections and who revealed evidence of urologic disease in the course of the present study. These obviously were patients with the most severe initial infections since 8 of the 13 were hospitalized, and in only one case was a concomitant pneumonia the probable cause for admission. As will be seen from the table, many of these patients had cultures which grew the organisms most commonly found in urinary tract infection, and in the follow-up study the same organisms were grown in 4 of 8 cases in which records were complete. Many of these patients had been admitted at the time of the recurrences and had had some urologic study and treatment at some time in the interim. None, however, had had any investigation or treatment within two years of the present study.

At the time of this study pyuria and positive cultures were found in 9 of the 13 cases. In two instances, the urinary tract infection was the only abnormality, the pyelograms being normal. It is probably worth while to record some of the case histories in this group with pyelographic findings.

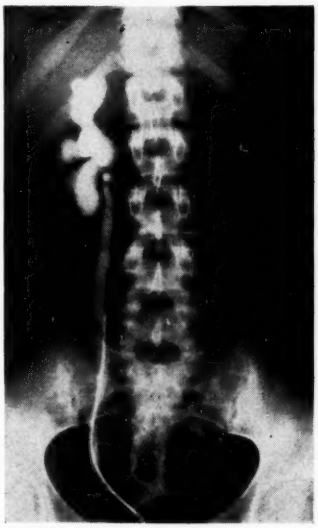

Fig. 4.—Retrograde study in Case 55 showing caliectasis and apparent ureteropelvic junction obstruction.

CASE 55.—The primary disease occurred at the age of two years with colon bacillus the infecting organism, and in the follow-up a similar organism was cultured. The patient had four recurrences with the same organism and two pregnancies, both complicated by pyelitis. Pyelographic findings are seen in Fig. 4, demonstrating dilation of pelvis and calyces with ureteropelvic junction obstruction. After repeated dilatation and Sulfathalidine therapy, the culture became negative. With subsequent pregnancy, however, she has had recurrence of infection. Apparently at no time during the twenty years from initial infection to the time of the present study had this patient's urine been sterile.

CASE 56.—In the eleven and one-half years between the initial infection and the present, this child had three recurrences and, as in Case 55, colon bacillus was the offending organism. Intravenous pyelograms and subsequent retrograde studies are seen in Figs. 5 and 6, showing double pelvis and ureter on the right with dilatation of both systems and posi-

tive cultures. Again, it had been seemingly impossible to eradicate the infection, in spite of several cystoscopies and local therapy for two years after the initial attack. The patient had not been seen for eight years at the time of this study.

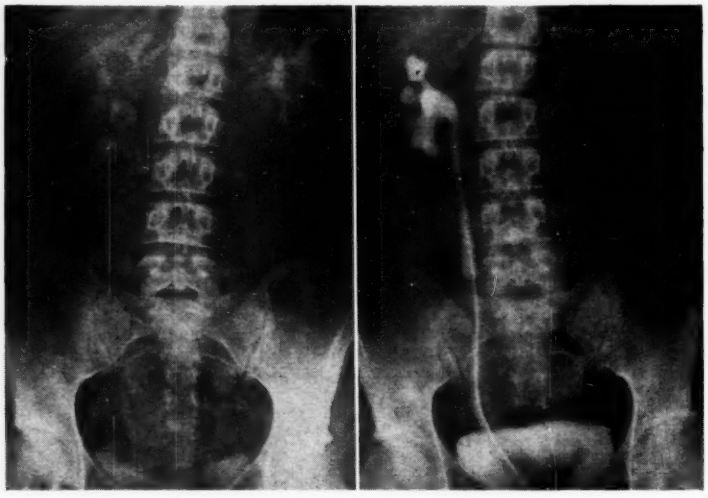

Fig. 5. Fig. 6.

Fig. 5.—Reduplication of right urinary tract in Case 56.
Fig. 6.—Retrograde study of the lower drainage system in Case 56, demonstrating mild caliectasis.

Fig. 7.—Marked hydronephrosis due to ureteropelvic junction obstruction found in Case 58.

CAES 58.—Here are demonstrated again the findings in a patient who had been seen at least three times in the seven years during the interim, with positive cultures and pyelographic evidence of upper tract disease. The first culture revealed only diphtheroids, but at cystoscopy the organism, as before, was a gram-negative bacillus. The pathology as seen in Fig. 7 is ureteropelvic junction obstruction felt to be due to an aberrant vessel. The family has refused to accept operative therapy up to the present.

CASE 59.—This patient presented the most remarkable x-ray changes seen in the entire series, with tremendous hydroureteronephrosis, reduced function, Flexner bacillus infection,

and mild azotemia. The pathology was recognized at the time of initial infection, but therapy has been unsuccessful in eliminating the infection or improving the status of the urinary tract. The x-ray findings are shown in Figs. 8 and 9. The patient is nevertheless relatively asymptomatic and leads a normal life.

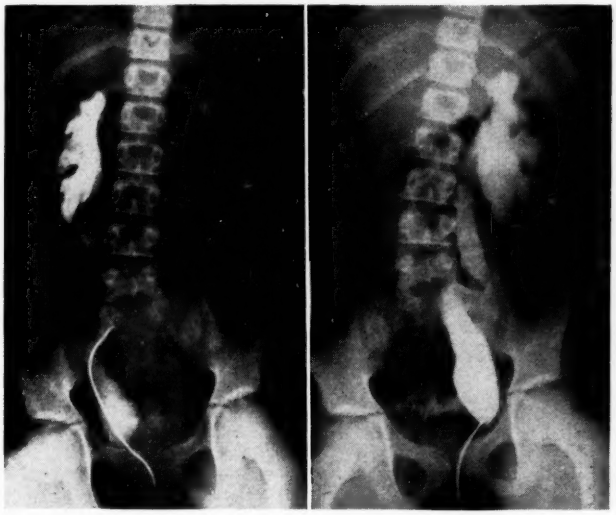

Fig. 8. Fig. 9.

Fig. 8.—Tremendous left hydronephrosis and hydroureter seen in Case 59.
Fig. 9.—Right retrograde study in Case 59 showing picture similar to that seen in Fig. 8.

Fig. 10.—Mild caliectasis and hydronephrosis noted by retrograde pyelography in Case 60.

CASE 60.—Pyelographic studies in this 22-year-old Negro woman shown in Fig. 10. She had had urinary tract infections with two of her three pregnancies. Again the offending organisms had apparently never been completely eradicated, although the patient was entirely asymptomatic.

Of interest in the interval history was the number of patients who had had urinary tract infection during pregnancy. As noted in Table VI, there were 16 pregnancies in Group I, i.e., those patients who had had only one episode of

urinary tract infection, and in only one case was the pregnancy complicated by urinary tract infection. In Group II, however, infection was found in 5 of 10 pregnancies. This is simply further evidence of the more serious significance of recurrent or persistent pyuria.

TABLE VI. COMPLICATIONS IN PREGNANCY

	NUMBER OF CASES	NUMBER OF PREGNANCIES	WITHOUT URINARY TRACT INFECTION	WITH URINARY TRACT INFECTION	PERCENTAGE WITH URINARY TRACT INFECTION
Group IA	37	12	12	0	0
Group IB	17	4	3	1	25.00
Group IIA	9	4	3	1	25.00
Group IIB	13	6	2	4	66.67

In 75 cases of pyelitis in pregnancy which occurred during the years 1947 to 1950, with 9,874 full-term pregnancies, there were 5 patients who had had urinary tract infections in childhood. These are briefly noted in Table VII.

TABLE VII. CASES OF URINARY TRACT INFECTION IN CHILDHOOD PRIOR TO PREGNANCY

1. Horshoe kidney with chronic pyelonephritis
2. Hematuria, albuminuria, pyuria at age 5 years, ? glomerulonephritis. Hydronephrosis, right
3. Pyelitis at age 2 years. Persistent infection. Hydronephrosis, right. Case 55
4. Pyelitis at age 7 years. Strictures. Intravenous pyelogram normal
5. Pyelitis at age 11 years. Hydronephrosis, right

In all but one of these, there is evidence of upper tract pathology at present, and the infection is of the chronic or recurrent and frequently asymptomatic variety, characteristic of the cases presented in this discussion. In 4 of the 5 the offending organism was of the colon group. No culture is recorded in the fifth case. Of the 10 pregnancies carried to term by these 5 patients, infections were noted in 8. Two pregnancies were not followed in the clinic.

Fifty-four of the 75 patients had had pregnancies other than the one recorded in this study. Forty had no evidence of urinary tract infection with the previous or succeeding pregnancies. Fourteen developed pyuria. No pathology was known to exist in 10 of the 14. Four revealed evidence of upper tract disease and these 4 had had urinary tract problems in childhood. Follow-up has been insufficient in the remaining 10 cases to justify any conclusion.

Comment

Urinary tract infection in girls is a relatively common disease. The common picture is one of a relatively mild febrile episode without localizing symptoms which responds readily to proper therapy, and hospitalization is not necessary. In the follow-up of this group of patients, little pathology will be found in the urologic study. It appears, however, from this study, that in spite of the benignity of the initial attack and general good health in later life, an appreciable minority of these cases show minimal pathology and the occasional case, severe damage. A majority of those patients with recurrent infection, especially if the initial episode was severe enough to warrant hospitalization, will reveal evidence of upper tract disease as indicated by the studies of Wharton, Gray, and Guild, and also by our results in Group IIB.

The general condition of the patient is certainly no index as to the presence or absence of urologic disease. Symptoms referable to the urinary tract again are rarely noted in this study and the absence of such symptoms is no criterion as to the condition of the urinary tract. Even urinalysis and culture are inadequate to eliminate abnormality.

It becomes increasingly apparent, then, that in order to rule out urologic pathology, all cases of urinary tract infection in childhood should have pyelographic study as part of the follow-up. This procedure is mandatory certainly if the patient has a persistent or recurrent pyuria.

The study re-emphasizes the importance of eliminating the infection as promptly as possible, and of making every effort to follow the patient to determine whether or not this is accomplished. Case 55, as well as several others, records the increased difficulty in eradicating organisms which have become well established over a long period of time. Such cases of chronic pyelonephritis are amazingly asymptomatic but, as is well known, often produce a shrunken, functionless kidney in later life.

Conclusions

1. Urinary tract infections in childhood warrant careful follow-up study, as indicated by the incidence of abnormality found in this series of unselected cases.

2. The interval between the time of study and the initial attack was not a factor in the severity of the disease.

3. Pathology was about twice as commonly found in those patients who had had recurrent infections as in those who had had only one episode.

4. Urinary tract infections were frequent complications of pregnancies which occurred in patients who had had recurrent disease and pathological abnormality but were uncommon in other groups.

5. Foci of infection were no more commonly found in patients with recurrent infections and/or pathology in the urinary tract than in those whose study was normal.

6. No instance of cardiovascular pathology was found in the entire group, with the exception of one blood pressure recording of 160/104 in a patient with a normal urinary tract and no infection.

7. Necessity for admission at the time of initial attack was a good indication of the severity of the infection and the possibility of pathology being present was greatly increased in this group.

8. Although most patients with mild initial infections and no recurrences revealed little pathology, the occasional case such as Case 2 demonstrates the necessity for thorough follow-up of all cases of urinary tract infection in children.

Reference

1. Wharton, L. R., Gray, L. A., and Guild, H. G.: J. A. M. A. **109**: 1597, 1937.

MULTIPLE UTEROTUBAL INSUFFLATIONS IN CASES OF STERILITY DUE TO TUBAL OCCLUSION

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(From Beth Israel Hospital)

MULTIPLE uterotubal insufflations exert more of a therapeutic influence in the resistant cases of tubal occlusion, than one or two insufflations. The purpose of this paper is to report a group of sterility cases that required multiple insufflations, i.e., six or more, to overcome the tubal obstruction, and in which pregnancy occurred within two months after the last Rubin test. In each case of this series, tubal occlusion was believed to be the sole cause for the sterility. All cases had shown tubal obstruction to gas at the maximum prescribed pressure of 200 mm. of Hg or higher, or to oil on the initial investigation.

In 1919, I. C. Rubin[1] first demonstrated the value of uterotubal insufflation as a diagnostic procedure in cases of sterility due to tubal occlusion. In the next 35 years, a large number of studies on this subject were reported. Most of these articles dealt with uterotubal insufflation for diagnosis; fewer stressed its therapeutic value. Little attention was given to the value of multiple tests in the treatment of tubal stenosis. In 1945, Dr. I. C. Rubin[2] reported on 590 cases of pregnancy occurring following insufflation in 3,200 sterility cases. In one case, he had to do 18 insufflations. J. Novak,[3] P. Titus,[4] and I. Stein,[5] among others have also reported successes with multiple insufflations. Reports on many repeated insufflations, in single cases, however, are rather infrequent and in the majority of cases two or three insufflations were the maximum number of tests performed on any one patient.

Procedure

Twenty-nine patients with sterility due to tubal obstruction, who had at least six or more therapeutic uterotubal insufflations, were selected. In each case, no other cause of sterility could be found. Insufflations were performed with carbon dioxide gas delivered under 15 pounds of pressure. The glass siphon meter was regulated to give two pulsations per minute (60 c.c. of carbon dioxide). Each test was run for five minutes, and a total of 300 c.c. of carbon dioxide was used in each case. All tests were performed between the third and seventh days after the end of the menstrual period. Each patient had a fluoroscopic examination in the erect position about 2 minutes after the completion of the test.

The following criteria were used as a standard for tubal patency sufficient for pregnancy to ensue:

1. Initial pressure did not go higher than 120 mm. of Hg on the graph.
2. Following the initial rise, the pressure fell immediately to normal (100 mm. of Hg) or less.

3. Either or both diaphragms had to be shown by fluoroscopy to be elevated at least ¾ to one inch or more, by the layer of carbon dioxide.

These 29 cases were selected because they were successful as far as pregnancy was concerned and they all fulfilled the criteria stated in this paper that were necessary for pregnancy to ensue. During this six-year period from which my cases were selected, about 500 insufflations were performed in sterility cases; these included tests performed for diagnosis and therapy. There were many cases in which the tubes were found patent on initial test or on the second or third attempt. They were found closed on the initial test in about 100 cases. Some of these patients did not return for more than one treatment, others were discouraged or disappointed at the lack of success after numerous insufflations and did not return for further treatment. The greatest number of insufflations performed on a single patient were 46 over a period of 7 years. Pregnancy did not occur in this case. At no time during the 7 years of testing in this case were the criteria indicative of normal tubal patency obtained.

The pertinent details of these cases are shown in Table I. A summary of these results is as follows:

10 cases required 6 uterotubal insufflations.
9 cases required 7 to 9 uterotubal insufflations.
4 cases required 10 to 15 uterotubal insufflations.
3 cases required 15 to 20 uterotubal insufflations.
3 cases required 20 to 30 uterotubal insufflations.

In the 29 cases presented, the average age of the patient was 28.5 years, the youngest being 22, and the oldest 36 years of age. There were 24 cases of primary sterility, and 5 cases of secondary sterility. The average duration of sterility was 33 months, the longest being 120 months, and the shortest, 18 months. These 29 patients had 35 pregnancies from which there were 21 living infants. Eight patients aborted, one twice. There were no tubal pregnancies. None of the living children were abnormal.

Comment

In order to increase our success in the therapeutic use of uterotubal insufflation, a distinction between tubal patency and patency of the tube sufficient for pregnancy to ensue was made. The elicitation of shoulder pain, or the auscultation of a tubal souffle, or the presence of a small amount of carbon dioxide under the diaphragm, is an indication that some degree of patency of the tube exists. In many cases, however, this degree of tubal patency may not be sufficient for the ovum or fertilized ovum to pass through. The conditions for tubal patency outlined in this paper, have permitted the ovum to migrate and pregnancy to follow in each case. The establishment of exact criteria for tubal patency sufficient for pregnancy to follow is important. The sole reliance on inaccurate criteria will hinder further efforts to open tubes and thus reduce the number of successes. The difference between success and failure in the treatment of tubal occlusion is often due to lack of definite criteria

TABLE I. SUMMARY OF SUBSEQUENT HISTORIES OF 29 PATIENTS WHO BECAME PREGNANT AFTER TUBAL INSUFFLATION

PATIENTS' INITIALS	AGE (YEARS)	YEARS MARRIED	DURATION OF STERILITY (YEARS)	TOTAL NO. OF INSUF-FLATIONS	DURATION OF TREATMENT	LAST RUBIN TEST	LAST MENSTRUAL PERIOD	OBSTETRICAL RESULTS	SUBSEQUENT OBSTETRICAL HISTORY
C. C.	26	2	1½	7	June 17, 1946–Dec. 23, 1946	Dec. 23, 1946	Dec. 14, 1946	Miscarriage at 2½ months	Had a girl May 18, 1948
R. G.	28	8	3	11	Aug. 2, 1944–May 31, 1945	May 31, 1945	July 4, 1945	Stillbirth, April 20, 1946	Had a boy May 2, 1947
A. H.	35	9	2	10	Sept. 27, 1948–June 1, 1949	June 1, 1949	Aug. 10, 1949	Miscarriage at 4½ months	Miscarriage at 3½ months
S. H.	27	4	2	6	March 20, 1950–Aug. 28, 1950	Aug. 28, 1950	Aug. 10, 1950	Boy June 2, 1951	
J. H.	29	8	3	22	Jan. 18, 1949–May 15, 1950	May 15, 1950	July 28, 1950	Girl May 4, 1951	Had a boy Aug. 30, 1952
B. J.	22	2½	2	7	June 23, 1948–Dec. 8, 1948	Dec. 8, 1948	Dec. 1, 1948	Boy Sept. 11, 1948	Had a boy July 26, 1951
N. K.	23	2	2	8	Sept. 10, 1943–April 26, 1944	April 26, 1944	April 18, 1944	Miscarriage at 3½ months	
P. K.	25	3	3	23	May 3, 1948–April 25, 1950	April 25, 1950	May 18, 1950	Girl Feb. 21, 1951	
R. K.	28	4	2	6	March 28, 1944–Oct. 30, 1944	Oct. 30, 1944	Nov. 30, 1944	Boy Sept. 19, 1945	
R. L.	27	3	2	6	Nov. 22, 1943–March 20, 1944	March 30, 1944	March 19, 1944	Boy Dec. 19, 1944	Had a boy May 3, 1947
E. N.	31	11	10	10	Nov. 4, 1946–Feb. 11, 1948	Feb. 11, 1948	March 3, 1948	Miscarriage at 2½ months	
C. P.	32	2	2	7	Oct. 17, 1947–Jan. 8, 1948	Jan. 8, 1948	Dec. 31, 1947	Boy Nov. 4, 1948	
I. R.	32	5	2	17	June 26, 1947–May 26, 1948	May 26, 1948	July 10, 1948	Miscarriage at 2½ months	

L. R.	25	2	2	6	Oct. 3, 1946–March 13, 1947	March 13, 1947	March 6, 1947	Boy Dec. 14, 1947	
E. S.	30	3	2	16	June 15, 1946–Oct. 10, 1947	Oct. 10, 1947	Oct. 28, 1947	Boy July 23, 1948	Had a girl Feb. 12, 1952
I. S.	25	6	2	8	Feb. 9, 1948–Sept. 30, 1948	Sept. 30, 1948	Oct. 19, 1948	Girl July 25, 1949	Had a boy July 14, 1949
R. S.	24	3	2	6	Oct. 7, 1946–March 15, 1947	March 15, 1947	March 3, 1947	Boy Dec. 29, 1947	Had a girl Nov. 18, 1951
R. S.	36	11	2	6	June 6, 1946–Nov. 8, 1946	Nov. 8, 1946	Jan. 2, 1947	Girl Oct. 6, 1947	
D. S.	32	7	5	6	April 15, 1948–Aug. 20, 1948	Aug. 20, 1948	Aug. 14, 1948	Girl March 20, 1949	Had a boy Dec. 15, 1950
R. O.	22	2	2	16	Jan. 15, 1949–July 20, 1950	April 25, 1950	May 18, 1950	Miscarriage at 4 months	
E. T.	30	4	3	7	Dec. 2, 1948–June 22, 1949	June 22, 1949	July 7, 1949	Girl April 27, 1950	
M. Z.	36	8	2	7	Nov. 20, 1947–May 24, 1948	May 24, 1948	June 10, 1948	Girl March 24, 1949	
R. Z.	30	6	2	6	Oct. 15, 1944–March 7, 1945	March 7, 1945	Feb. 26, 1945	Girl Dec. 18, 1945	
C. W.	28	5	3	6	July 8, 1947–Dec. 3, 1947	Dec. 3, 1947	Nov. 25, 1947	Girl Sept. 2, 1948	Had a boy Jan. 30, 1951
S. Y.	30	4	2	8	Oct. 10, 1943–May 18, 1944	May 8, 1944	May 24, 1944	Girl Feb. 19, 1945	
S. D.	29	7	2	28	Jan. 20, 1949–Sept. 10, 1951	Sept. 10, 1951	Oct. 7, 1951	Boy July 24, 1952	
R. W.	22	2	2	6	July 10, 1950–Feb. 16, 1951	Feb. 16, 1951	March 7, 1951	Boy Dec. 17, 1951	
M. F.	36	10	7	7	Oct. 4, 1950–Sept. 18, 1951	Sept. 18, 1951	Oct. 2, 1951	Girl June 22, 1952	
N. S.	27	4	3	10	Oct. 6, 1949–Nov. 9, 1950	Nov. 9, 1950	Nov. 1, 1950	Miscarriage at 5 months	Had a boy May 8, 1952

for tubal patency sufficient for pregnancy to ensue. It is obvious that the tubes may be open, but not sufficiently so for the unfertilized or fertilized ovum to migrate through. When uterotubal insufflations are discontinued before this degree of patency is obtained, the patient has little chance to conceive.

The question often arises, in cases where two or three or even six insufflations have failed to open the tubes or only partially opened them, whether treatment should be discontinued. The answer to this question is difficult. It could be made easier if we had results in many large series of multiple-insufflation tests in individual cases with which to compare them. The results in our series of cases encourage us to continue as long as the patient cooperates. Had we stopped sooner, or had the patient not returned often enough in any of our cases, it is felt certain that our results would have been less successful.

Conclusions

1. Twenty-nine cases of tubal obstruction have been presented in which pregnancy occurred within two months after the last uterotubal insufflation. In each of these cases, at least six insufflations had been performed.

2. Therapeutic uterotubal insufflations should be continued until the tubes are opened sufficiently for the migration of the ovum.

3. Criteria for tubal patency adequate to allow pregnancy to ensue are presented.

4. Many more successes in cases of sterility due to tubal stenosis can be obtained if the treatment is not discontinued after one, two, or three uterotubal insufflations.

5. In our hands, uterotubal insufflations have yielded more successes and fewer complications than plastic operations on the tube.

6. Uterotubal insufflation, performed properly and repeated at stated intervals as long as the patient cooperates, should greatly help to overcome tubal obstruction as a cause of sterility, even in the more resistant cases.

References

1. Rubin, I. C.: Uterotubal Insufflation, St. Louis, 1947, The C. V. Mosby Company.
2. Rubin, I. C.: Uterotubal Insufflation, St. Louis, 1947, The C. V. Mosby Company.
3. Novak, J.: Wien. klin. Wchnschr. 35: 789, 1922.
4. Titus, P.: Atlantic M. J. 30: 216, 1927.
5. Stein, I.: S. Clin. North America 7: 777, 1927.

ALKALINE PHOSPHATASE IN VAGINAL BIOPSIES

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THE phosphatases are enzymes whose function is that of hydrolyzing organic esters of phosphoric acid, thereby liberating inorganic phosphate. Alkaline phosphatase is a phosphomonesterase with optimum activity at a pH range of about 9.0 to 10.0. Like other phosphatases it is activated by magnesium salts. The roles played by this enzyme in food absorption, dephosphorylation within the liver, muscle metabolism, reabsorption of glucose by the renal tubules, and deposition of lime salts within the bones are well known. The most widely used histochemical techniques for staining are those of Gomori[1] and Takamatsu.[2]

The bulk of the work pertaining to alkaline phosphatase (AP) in the female genital tract has been concentrated on the endometrial changes during the menstrual cycle[3, 4] and during pregnancy.[5] It has been noted that AP activity is most evident during the follicular phase and less so during the progestational phase of the human cycle and that AP disappears several days before the onset of menstruation. It has not been demonstrated in the glands or decidual stroma of the gravid uterus although it is present in the capillary endothelium.[5, 6] Blood levels at term, however, reach three times the normal nonpregnant values.[7] The enzyme is found in cases of endometrial hyperplasia and in endometrial adenocarcinoma; in the latter, it exists in inverse ratio to the degree of tumor activity.[8] The myometrium does not contain AP in appreciable amounts.[9]

With respect to the ovary, Corner[10] states that the human theca interna contains AP which is lost within a few days after ovulation. In rat corpora lutea,[11] AP increases progressively during the course of pregnancy.

According to Wislocki, Bunting, and Dempsey[12] the enzyme is encountered irregularly during the human menstrual cycle in the cervical glands and cervical surface epithelium and is augmented during gestation, but Hedberg[13] demonstrated high phosphatase activity in the columnar cells during the proliferative phase of the menstrual cycle and lower activity during the progestational phase. In the stratified squamous epithelium of the portio, AP is said to be lacking.[12] This is somewhat surprising because of the similarity of this area to the vaginal epithelium where, according to our findings, AP is found constantly during the cycle.

The presence of AP has not been well studied in the vaginal tract. An increase of AP with the injection of estrogen has been noted in the vaginal mucosa of mice.[14, 15] Ayre and Millar[16] have reported on Gomori's technique

applied to more than 1,500 human benign and malignant vaginal smear preparations and correlated their work with some biopsy studies. Although we too have used essentially the same method of enzyme determination, we are well aware that it has been criticized as not sufficiently reliable for indicating intracellular enzyme sites.[17, 18]

Material and Methods

Our material consists of 148 biopsies taken from the midvaginal area of 50 women. Of these, 19 were in the childbearing era, 16 were pregnant, 4 were puerperant, and 11 were postmenopausal. The vaginal biopsies were taken usually by the punch method, occasionally with an Allis forceps and knife. An effort was made to obtain both epithelium and subepithelial connective tissue. Bleeding was rarely troublesome and was more likely to be so when the biopsy was taken from a gravid patient; it was invariably and easily controlled by packing with a hemostatic gauze. The biopsies were immediately placed in cold 80 per cent alcohol and then stained by the Wachstein modification[19] of the Gomori technique. The general principle of this method is the splitting of glycerophosphates by the enzyme in the tissue section, the phosphate being rendered insoluble by calcium. The calcium phosphate is then changed to a visible form by adding cobaltous nitrate to make white cobalt phosphate which is subsequently converted to black cobalt sulfide by the addition of ammonium sulfide. Glycogen staining was done on separate specimens by the Best carmine method. In the beginning of the study a few "control" biopsies were also stained with hematoxylin and eosin. Results for AP were tabulated as reported by Arzac and Blanchet[4]:

0 Negative reaction.
\+ Positive reaction in capillaries only.
++ Positive reaction in nucleoli also.
+++ Positive reaction in nuclei.
++++ Positive reaction in cytoplasm.

Results and Comment

In the mature vaginal epithelium of 19 women from whom biopsy specimens was taken at various times of the cycle, the enzyme was found to be concentrated in the nuclei and also the cytoplasm of the basal layers and in the papillary blood vessels. The superficial squamous cells also contained the enzyme in both the nucleus and cytoplasm but, with increasing cornification, the black precipitate tended to disappear. There was some staining of the stromal cells, most marked in the nuclei. We could find no great variation during the course of the menstrual cycle although there seemed to be slightly more AP noted in the latter half of the cycle. The enzyme was least discernible in the epithelium in the immediate premenstrual time, at least in two cases.

In biopsy specimens taken during different months of pregnancy (Fig. 1) from 16 women, the AP content rose quite rapidly to 3 plus and even to 4 plus. We did not notice a decrease in the last month of pregnancy as has been described in vaginal smears stained for AP at this time.[16] AP tended to be scant in the immediate postpartum period.

In the 11 postmenopausal women, AP varied from 0 to 4 plus and without any particular relationship to the number of years after the last menses. In

general, however, AP tended toward disappearance (1 plus to 2 plus) as age increased (Fig. 2). Estrogen administered locally produced the well-known histologic changes and increased the amount of AP present. Progesterone given parenterally to two castrates had no demonstrable effect, nor did testosterone.

The glycogen determinations turned out as would be expected,[20] namely, a slight increase at the midcycle, highest values in pregnancy, and scant to absent in the postmenopausal vagina. There was no regular relationship between AP activity and the amount of glycogen found histologically; whereas glycogen increased with cell cornification,[20] AP decreased. It is interesting that in the human endometrium, glycogen deposition seems to depend upon progesterone while in the vaginal epithelium this is an estrogenic effect. AP, on the other hand, seems to depend on estrogenic stimulation in both the endometrium and vagina.

Fig. 1.

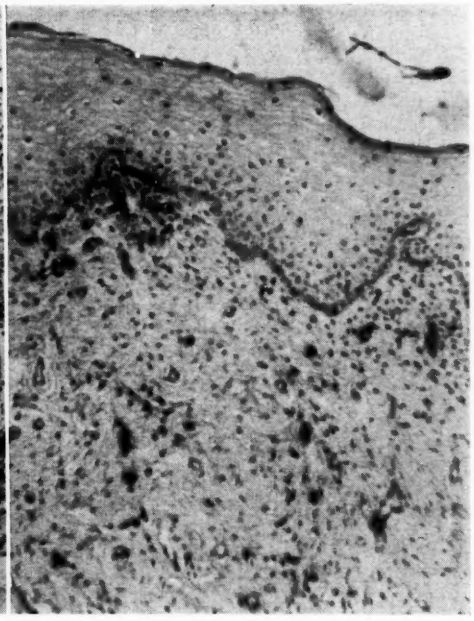

Fig. 2.

Fig. 1.—Vaginal biopsy stained for alkaline phosphatase from a patient in the third month of pregnancy. Note concentration in the blood vessels of subepithelial connective tissue and in the basement layer of the epithelium.

Fig. 2.—Vaginal biopsy stained for alkaline phosphatase from a 59-year-old postmenopausal woman. Note less concentration of the enzyme in comparison with Fig. 1.

The exact function of AP in the vaginal epithelium is only conjectural. The primary action of the phosphatases is to catalyze the hydrolysis of phosphoric ester; it may therefore be significant in the hydrolysis of glucose-phosphates during glycogen metabolism. It may also be related to protein anabolism or may have an important role at the site of active solute transfer (glucose?) across cell boundaries.[21] It probably has little or no direct relation to lactic acid formation.

Summary

1. Alkaline phosphatase is found in the vaginal mucosa mainly in the basal layers of the epithelium and in the papillary blood vessels.

2. There is little cyclic change noticed although it seems the concentration of alkaline phosphatase is greater during the secretory phase.

3. The greatest amounts of alkaline phosphatase are found during pregnancy, the least amounts after the menopause.

4. The exact function of alkaline phosphatase in the vaginal mucosa is unknown at present.

Addendum.—Since this paper was submitted for publication, we have found an article in the Italian literature reporting similar findings by G. Sani[22] on "Alkaline Phosphatase in the Human Vagina in Relation to Sex Hormones."

References

1. Gomori, G.: Proc. Soc. Exper. Biol. & Med. **42**: 23, 1939.
2. Takamatsu, H.: Tr. Soc. path. jap. **29**: 492, 1939.
3. Atkinson, W. B., and Elftman, H.: Endocrinology **39**: 30, 1947.
4. Arzac, J. P., and Blanchet, E.: J. Clin. Endocrinol. **2**: 365, 1942.
5. Wislocki, G. B., and Dempsey, E. W.: Am. J. Anat. **77**: 365, 1945.
6. Dempsey, E. W., and Wislocki, G. B.: Am. J. Anat. **80**: 1, 1947.
7. Speert, H., Graff, S., and Graff, A. M.: Am. J. Obst. & Gynec. **59**: 148, 1950.
8. Atkinson, W. B., and Gusberg, S. B.: Cancer **1**: 248, 1948.
9. Kabat, E. A., and Furth, J.: Am. J. Path. **17**: 303, 1941.
10. Corner, G. W.: In discussion on Atkinson, W. B., in Engle, E. T.: Menstruation and Its Disorders, Springfield, Ill., 1950, Charles C Thomas, p. 3.
11. Meyer, R. K., and McShan, W. H., in Engle, E. T.: Menstruation and Its Disorders, Springfield, Ill., 1950, Charles C Thomas, p. 62.
12. Wislocki, G. B., Bunting, H., and Dempsey, E. W., in Engle, E. T.: Menstruation and Its Disorders, Springfield, Ill., 1950, Charles C Thomas, p. 23.
13. Hedberg, G. T.: Gynaecologia **129**: 239, 1950.
14. Jeener, R.: Nature **159**: 578, 1947.
15. Kamell, S. A., and Atkinson, W. B.: Proc. Soc. Exper. Biol. & Med. **68**: 537, 1948.
16. Ayre, W. B., and Millar, B.: Cancer **4**: 159, 1951.
17. Feigin, I., Wolf, A., and Kabat, E. A.: Am. J. Path. **26**: 647, 1950.
18. Novikoff, A. B.: Science **113**: 320, 1951.
19. Wachstein, M.: J. Lab. & Clin. Med. **31**: 1, 1946.
20. Rakoff, A. E., Feo, L. G., and Goldstein, L.: Am. J. Obst. & Gynec. **4**: 467, 1944.
21. Bradfield, J. R. G.: Biol. Rev. **25**: 113, 1950.
22. Sani, G.: Quad. clin. ostet. ginec. **7**: 247, 1952.

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DIAGNOSTIC TRANSABDOMINAL PNEUMOPERITONEUM IN CHILDREN

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THE diagnostic value of transabdominal pneumoperitoneum in children was recently demonstrated by us before the American Academy of Pediatrics and reported in a recurrent communication[1] in the *American Journal of Diseases of Children*. Because we believe that the value of this procedure in the pediatric age group is not fully realized by gynecologists and radiologists, as well as by pediatricians, and because it can be performed in any hospital, a report of our technique and further experiences may be of aid to these specialty groups.

Our interest in using this technique resulted from the facts that even though pelvic examination in the adult may be satisfactory, in the infant or older child (or even the virgin adult) bimanual examination may be physically impossible or impractical. In such patients, therefore, pneumoperitoneum may be of help in determining the presence of pelvic anomalies and other gross pathologic conditions. Furthermore, pneumoperitoneum may be of considerable aid when it appears that a clinical diagnosis cannot be established without laparotomy and when laboratory data are inconclusive.

Diagnostic pneumoperitoneum is not new and was first introduced by Orndoff[2] in 1919 and subsequently in 1921 by Van Zwaluwenburg and Peterson,[3] Alvarez,[4] and Case.[5] Over the subsequent years several articles appeared in the literature, emphasizing not only diagnostic potentialities, but improvements in technique.[6-16] None of these reports suggested its use in children. In spite of these articles, the method has not received a wide degree of popularity, probably because dangers and contraindications of induced pneumoperitoneum have been overemphasized and because its diagnostic possibilities have not been appreciated. Through the efforts of Dr. Irving F. Stein, a pioneer in this field, and his co-workers at Michael Reese Hospital, the technique and diagnostic importance of induced pneumoperitoneum has been accepted by many members of the Department of Gynecology.[7, 14, 17] We have adapted the Stein technique for children, and to date have successfully used this method in a number of normal children and twenty-one with various sex-endocrine disturbances, the youngest of whom was 11 weeks of age.*

*One of the cases (Case 5) included in our series was recently published in detail by Levin, Rambar, and Shapiro[18] and is abstracted with the permission of the authors.

Material and Methods

Pneumoperitoneum has been performed on several normal female children of various ages so that for comparative purposes pelvic abnormalities could be demonstrated radiographically with fewer errors in interpretation. The procedure is contraindicated (1) if the patient has an active intraperitoneal inflammatory process, (2) if there is reason to suspect adhesion of bowel to the parietal peritoneum at the site of the puncture, (3) if the patient has any cardiac and/or respiratory embarrassment, or, (4) if a systemic infection is present.

Prior to pneumoperitoneum, diagnostic studies were performed on all patients with sex-endocrine disturbances according to their individual problems and with the laboratory diagnostic facilities available to us at the time of the study. The various procedures are as follows:

1. History and physical examination.
2. Measurements: weight, height span, symphysis-vertex, symphysis-sole.
3. Laboratory determinations: basal metabolic rate, fasting blood sugar; serum cholesterol, cholesterol esters; intravenous insulin tolerance test.
4. Hormone excretion: urinary 17-ketosteroids, urinary pregnandiol.
5. Vaginal smear for estrogen activity (Shorr stain).
6. X-ray studies: skull (sella turcica), bone age, perirenal air insufflation, pneumoperitoneum.
7. Endometrial biopsy.

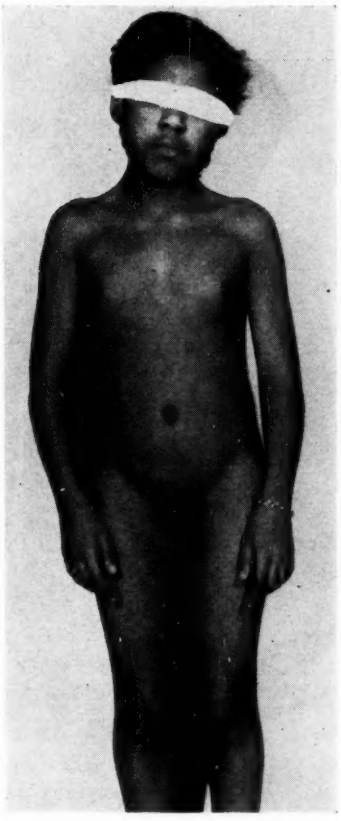
For a detailed evaluation of laboratory diagnostic methods, Wilkins',[19] *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence* should be consulted.

Technique for Transabdominal Pneumoperitoneum

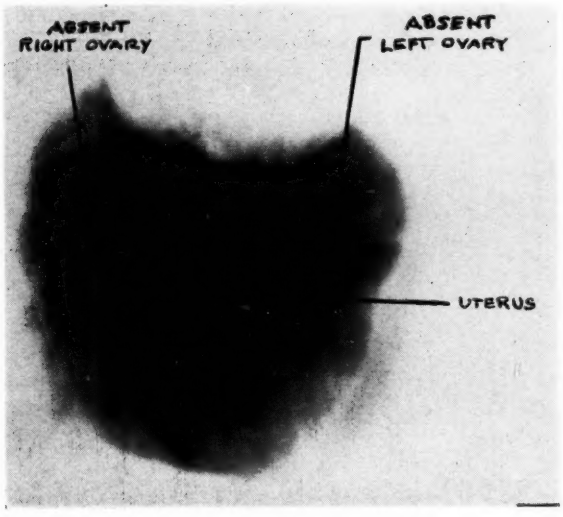
A urologic radiographic table, as described by Stein and Arens,[17] is used and the following procedures are carried out:

1. High cleansing enema on morning of procedure.
2. No breakfast.
3. Intramuscular administration of 25 to 100 mg. of meperidine (Demerol) according to weight. Opiates are not administered to infants under 1 year of age; instead, sedation is accomplished with either Seconal or Nembutal rectal suppositories, 1 to 2 grains.
4. Bladder catheterization.
5. Transabdominal puncture 1 in. (12.5 cm.) below and 1 in. to the left of the umbilicus using a 20-gauge spinal needle with stylet. The needle is inserted perpendicular to the abdominal wall until the peritoneum is penetrated. A sudden decrease in resistance to the advancing needle signifies penetration. The depth at which this will occur depends upon the thickness of the abdominal wall.
6. Introduction of 300 to 700 c.c. (average 500 c.c.) of carbon dioxide* under 10 to 20 mm. Hg pressure using a simple apparatus attached to a carbon dioxide cylinder.[1]
7. Prompt placement of patient in modified knee-chest position on radiographic table with the Potter-Bucky diaphragm close to the abdominal wall.[1] In the case of small infants, an ordinary small feather pillow is used on top of the table and under the infant so that the desired position may be obtained.

*One hundred cubic centimeters of oxygen was used instead of carbon dioxide in the case of an 11-week-old infant. Oxygen is used in all small infants as the rapid absorption of carbon dioxide does not permit repeating films if this is necessary without introducing more gas.[18] All carbon dioxide is absorbed within 12 to 24 hours, whereas oxygen is absorbed considerably more slowly. Some of the patients had a minimum amount of discomfort consisting of shoulder pain of several hours' duration. No untoward complications have resulted from introduction of either gas.



A.



B.

Fig. 1.—Case 1, P. L., aged 14 years. Ovarian agenesis.

A, Photograph of patient. Dwarfism (height 53 inches, weight 77 pounds), photograph taken after estrogen therapy showing slight breast development, no axillary hair, sparse pubic hair, infantile vulva and vagina.

B, Pneumoperitoneum showing absence of ovaries and minute uterus.

8. X-ray factors: 65 to 70 kv., 100 Ma., 1/10 second.

Clinical Observations

Transabdominal pneumoperitoneum was performed in 21 patients with various sex-endocrine disturbances; the clinical classification of these is indicated in Table I.

TABLE I. CLINICAL CLASSIFICATION

1. Ovarian agenesis	8 cases
2. Hypopituitarism, primary	1
3. Hypoovarianism	2
4. Cystic ovary	1
5. Sexual precocity (constitutional)	3
6. Pseudohermaphroditism	5
7. Polycystic ovaries	1
Total	21 cases

From this group the following cases are presented with a brief clinical summary:

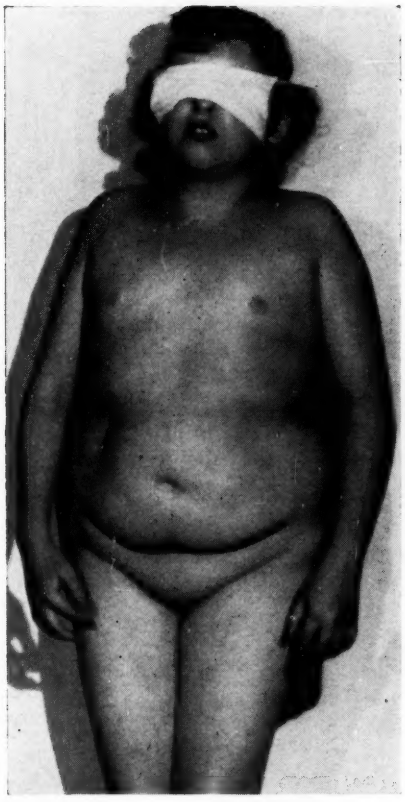
CASE 1.—*Ovarian Agenesis:* A 14-year-old Negro girl with the presenting complaints of failure to grow and failure of breast development. Height 53 inches, weight 77 pounds. There was fine hair on the face, no axillary hair and sparse pubic hair. The external genitals were infantile. There was slight webbing of the neck. Bone age was normal. Pneumoperitoneum revealed absence of ovaries and a minute uterus (Fig. 1).

CASE 2.—*Primary Hypopituitarism:* A 19-year-old white girl with complaints of failure to grow and failure to menstruate. Height 52 inches, weight 85 pounds. She was obese and her appearance was juvenile. Her body proportions were normal. There was sparse axillary and pubic hair, the genitals were juvenile and the breasts hypoplastic. The bone age was slightly retarded. She showed increased sensitivity to intravenous insulin. Serum protein iodine was 5.5 μg per 100 c.c.; the basal metabolic rate was -3.5 per cent. Vaginal smears showed no evidence of estrogen activity. Pregnandiol excretion was 0.05 mg. in 24 hours. Clinical diagnosis: probable primary hypopituitarism, possibly ovarian agenesis. Pneumoperitoneum revealed small ovaries and an infantile uterus (Fig. 2). Final diagnosis: primary hypopituitarism.

CASE 3.—*Constitutional Sexual Precocity:* A 7¾-year-old white girl with the complaints that breasts had been developing and pubic hair had appeared during the past nine months. She was taller than average and her appearance was that of an adolescent girl. The breasts were of moderate size, the areola pigmented, and pubic hair was abundant. The vulva was pigmented, the fossa navicularis developed, and the vagina rugated. The bone age was 12 to 14 years. Vaginal smears showed high estrogen activity. Pneumoperitoneum revealed normal adolescent uterus and ovaries (Fig. 3).

CASE 4.—*Cystic Ovary:* A 13-year-old Negro girl complained of excessive vaginal bleeding for three weeks followed by failure to menstruate for two months. Height 62 inches, weight 116 pounds. Her development was normal although her features were mature. Vaginal smears showed persistent high estrogen activity. Pneumoperitoneum demonstrated an enlarged right ovary, believed to be cystic (Fig. 4).

CASE 5.—*Female Pseudohermaphroditism:*[18] A 5-year-old child whose parents complained of the presence of pubic hair, and abnormal genitals and undescended testes observed at birth. The child appeared taller than normal. There was abundant, coarse pubic hair, few axillary and chest hairs; there was a penislike structure with a urethral opening at the base of the shaft, and a bifid scrotal-appearing structure with rugated folds. There were no masses palpated in this area nor in the inguinal regions. The bone age was 14



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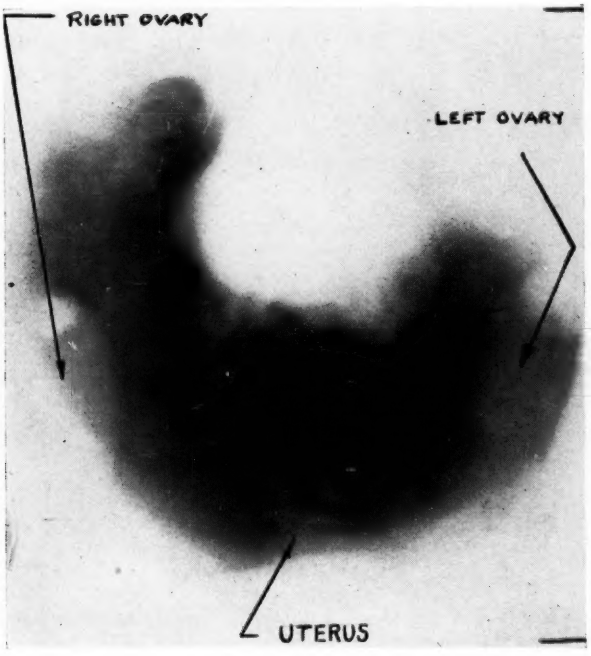

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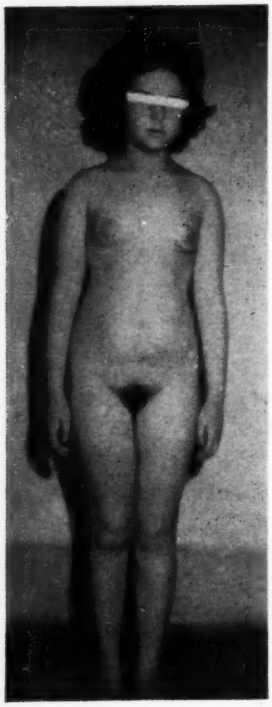
Fig. 2.—Case 2, E. Z., aged 19 years. Hypopituitarism.

A, Photograph of patient. Dwarfism (52 inches, 85 pounds), juvenile appearance, absent secondary sex characteristics, obesity.

B, Pneumoperitoneum showing juvenile ovaries and infantile uterus.



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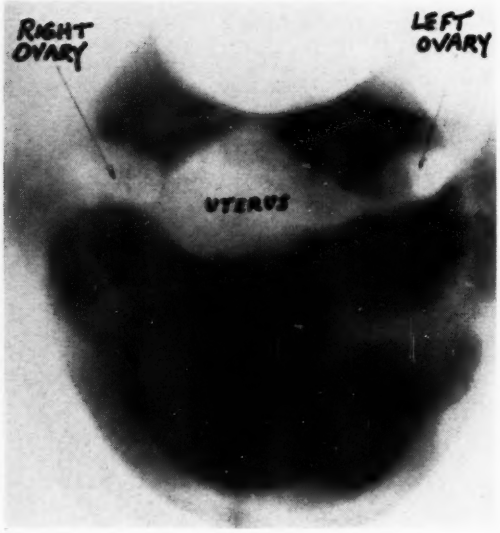

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Fig. 3.—Case 3, M. F., aged 7¾ years. Constitutional sexual precocity. *A*, Photograph of patient. Adolescent breasts, abundant pubic hair. *B*, Pneumoperitoneum showing normal adolescent ovaries and uterus.

A.

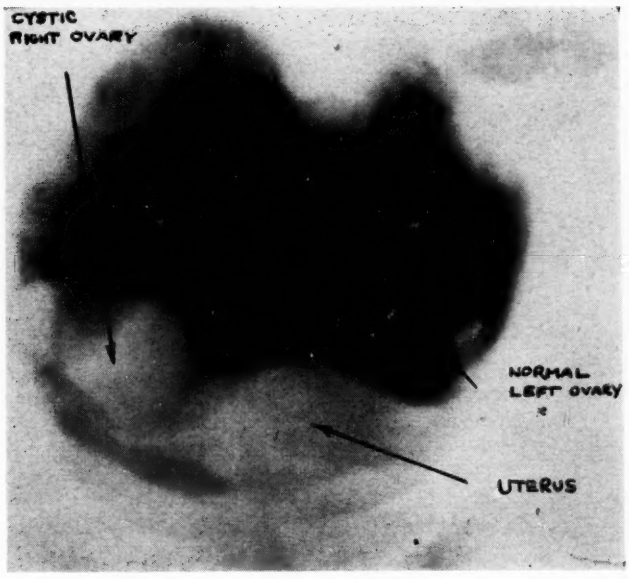

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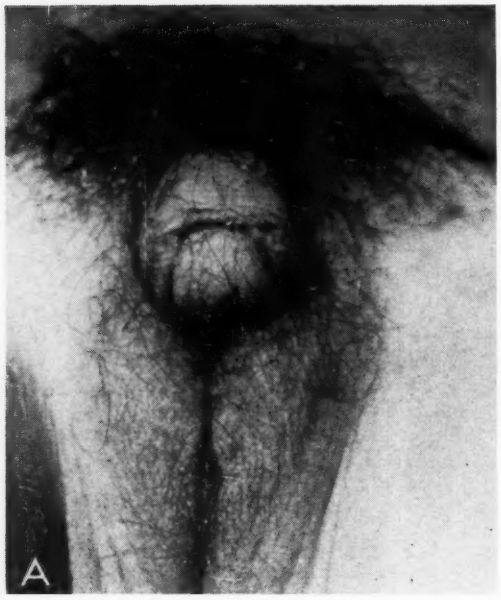
Fig. 4.—Case 4, E. J., aged 13 years. Probable cystic right ovary.

A, Photograph of patient. Height 62 inches, weight 116 pounds. Normal female development.

B, Pneumoperitoneum showing enlarged right ovary.



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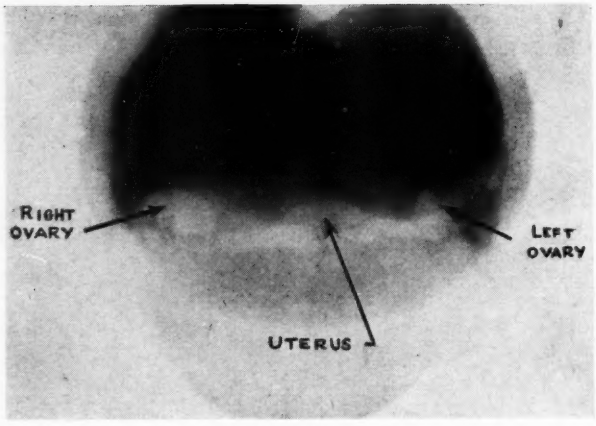


B.

Fig. 5.—Case 5, S. S., aged 5 years. Female pseudohermaphrodite; adrenogenital syndrome.

A, Photograph of genitals. Coarse, abundant pubic hair, penislike structure with urethral opening at base of shaft, bifid scrotumlike structure, rugated scrotal folds.

B, Pneumoperitoneum showing presence of ovaries and uterus.

years. Pregnandiol excretion was 99 mg. in 24 hours. Perirenal air insufflation showed normal-appearing adrenals. A clinical diagnosis of adrenocortical syndrome was made. Pneumoperitoneum demonstrated uterus and ovaries (Fig. 5). Final diagnosis: female pseudohermaphroditism, adrenocortical syndrome.

CASE 6.—*Probable Male Pseudohermaphroditism:* A 21-month-old white infant with abnormal genitals noted at birth. The height and weight were average for the age. Hypospadius or a hypertrophied clitoris was present. The phallus was 1 cm. in length, adherent posteriorly. A dimple 1 cm. below the urethral orifice, located at the base of the phallus, was present. There was a questionable vaginal meatus. No urogenital sinus could be demonstrated. There was an empty bifid scrotum. A pea-sized mass was palpated in the right inguinal region, the left was empty. There was no sexual hair; 17-ketosteroid excretion was not determined. Pneumoperitoneum showed absence of female pelvic structures (Fig. 6). A final diagnosis awaits exploration of the inguinal regions.

A.

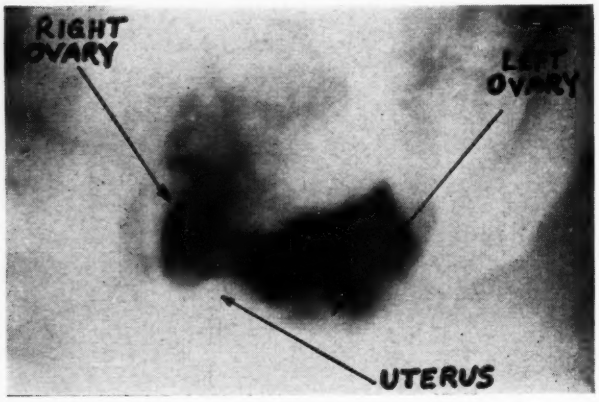
B.

Fig. 6.—Case 6, G. G., aged 21 months. Probable male pseudohermaphrodite.
A, Photograph of external genitals. Hypospadius or hypertrophied clitoris. Urethral opening at base of shaft, bifid empty scrotumlike structure. No sexual hair.
B, Pneumoperitoneum showing absence of female pelvic structures.

CASE 7.—*Female Pseudohermaphroditism:* An 11-week-old infant with abnormality of the external genitals noted at birth. Length 23 inches, weight 10 pounds. The infant appeared older than the chronological age. The phallus was larger than normal, measuring 1.5 cm. in length, and was bound down between two flabby structures resembling enlarged labia majora or an underdeveloped bifid scrotum. The urethral opening was 1 cm. below the base of the phallus. Rectal examination was unsatisfactory. An x-ray of the wrists showed two carpal centers. The blood serum electrolytes were within normal limits; 17-

A.

B.



C.

Fig. 7.—Case 7, R. Mc., aged 11 weeks.

A, Infant appears older than 11 weeks. Abnormal external genitals.

B, Large phallus; bifid scrotumlike structure, rugated folds; urethral opening at base of phallus.

C, Pneumoperitoneum showing presence of uterus and ovaries.

ketosteroid excretion was 1.9 mg. (normal 0-5 mg.[19]). A clinical diagnosis of adrenocortical syndrome was made. Pneumoperitoneum revealed ovaries and uterus (Fig. 7). Final diagnosis: female pseudohermaphroditism, adrenocortical syndrome.

Summary and Conclusions

In some sex-endocrine disturbances, detailed physical examination as well as available laboratory studies may be diagnostically inconclusive. In such cases transabdominal pneumoperitoneum may aid in establishing the clinical diagnosis and thus avoid laparotomy. The method is of special value in the study of children with such disturbances because of the difficulty of adequate pelvic examination. Furthermore, early diagnosis is desirable in order to plan future medical and/or surgical management.

The technique consists of introducing a measured amount of carbon dioxide or oxygen into the peritoneal cavity and then visualizing roentgenographically the outline of the pelvic viscera. Several normal infants and children and 21 with various sex-endocrine disturbances have been studied by this technique. The latter cases consisted of ovarian agenesis, hypopituitarism, hypoovarianism, cystic ovary, sexual precocity, pseudohermaphroditism, and polycystic ovaries.

References

1. Kunstadter, Ralph, Guterman, Henry S., and Tulsky, Alex: Am. J. Dis. Child. **86**: 275, 1953.
2. Orndoff, B. H.: J. Roentgenol. **2**: 265, 1919.
3. Van Zwaluwenburg, J. G., and Peterson, R.: Am. J. Roentgenol. **8**: 12, 1921.
4. Alvarez, W. C.: Am. J. Roentgenol. **8**: 71, 1921.
5. Case, J. T.: Am. J. Roentgenol. **8**: 714, 1921.
6. Stein, A., and Stewart, W.: Ann. Surg. **70**: 95, 1919.
7. Stein, I. F., and Arens, R. A.: Radiology **7**: 326, 1926.
8. Peterson, R.: J. A. M. A. **78**: 397, 1922.
9. Lewis, B. O.: Am. J. M. Sc. **211**: 84, 1946.
10. Sante, L. R.: Southwestern Med. **11**: 529, 1927.
11. Faulkner, W. B., Jr.: Am. J. Roentgenol. **45**: 72, 1941.
12. Martin, C. L.: Am. J. Roentgenol. **37**: 633, 1937.
13. Rubin, I. C.: Am. J. Roentgenol. **8**: 120, 1921.
14. Stein, I. F.: In Soskin, S., editor: Progress in Clinical Endocrinology, New York, 1950, Grune & Stratton, p. 374.
15. Maxfield, J. R., Jr., and McIlwain, A. J.: Radiology **42**: 346, 1944.
16. Maxfield, J. R., Jr.: J. A. M. A. **146**: 920, 1951.
17. Stein, Irving F., and Arens, Robert A.: Am. J. Obst. & Gynec. **63**: 1169, 1952.
18. Levin, Bertram, Rambar, Alwin C., and Shapiro, Irving J.: Am. J. Roentgenol. **69**: 948, 1953.
19. Wilkins, Lawson: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, Ill., 1950, Charles C Thomas.

VAGINITIS, DUE TO CANDIDA (MONILIASIS), TREATED WITH A BENZOTHIAZOLE DERIVATIVE*†

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SEVERAL reports[1-6] have indicated that Asterol dihydrochloride is useful in the treatment of various types of fungous infections involving the skin. It possesses advantages over other medicaments by virtue of being colorless, odorless, stable, and soluble in a variety of diluents. It seldom causes primary cutaneous irritation; it has a low index of allergic sensitization; and no toxicity has been observed in persons over 4½ years of age.[7, 8, 9, 10] These facts warranted its trial in the treatment of vaginal moniliasis. The experience gained in the care of 65 patients is the subject of this report.

Selection of Cases

Vaginitis is seldom etiologically simple, but results from the interaction of microbiologic and chemical factors; consequently, it is difficult to evaluate a specific medicament against a specific pathogenic organism. It is well established that monilial organisms (Candida species) are present intravaginally in a large percentage‡ of women, the majority of whom remain asymptomatic. The results of a survey made in our clinics during this study are given in Table I. To eliminate as many variables as possible in the present study, only those cases were included in which moniliasis was either the sole apparent cause of symptomatic vaginitis, or was overwhelmingly predominant over all other factors. These criteria were employed in selecting our cases: first, the clinical observation of patches resembling "thrush" on the vulvar or vaginal mucous membrane; second, the presence of the typical cheeselike discharge; and third, the presence of monilial organisms in profusion with little or no evidence of other pathogenic organisms. Sixty-five cases which fulfilled these conditions were studied.

*Asterol dihydrochloride, Hoffmann-La Roche, Inc., Nutley, N. J. With regard to this drug Wilson, Levitt, and Plunkett[6] state the following: "Asterol[R] is a substituted benzothiazole, specifically the dihydrochloride of 2-dimethylamino-6-(beta-diethylamino ethoxy) – benzothiazole. It is a white crystalline substance soluble in alcohol and water. A 5% solution has a pH of approximately 2.0. The toxicity for mice is low, the LD_{50} being 0.375 grams per kilo by the subcutaneous route and 0.5 grams per kilo by oral administration.

"Several other substituted benzothiazoles have found application as fungistatic agents in rubber and leather preservation and in agriculture; none was found to be significantly effective against dermatophytes. Conversely Asterol[R] is not fungistatic for such organisms as Penicillium or Aspergillus but is highly effective against the pathogenic species of importance in dermatology. Its antibacterial action was found to be negligible."

†The cooperation of the Los Angeles City Health Department (George M. Uhl, Health Officer) is gratefully acknowledged.

‡Of all patients with symptoms of vaginitis or discharge examined during this study, 61.2 per cent of the pregnant women and 45.4 per cent of the nonpregnant women and of all patients without these symptoms, 30.2 per cent of pregnant women and 46 per cent of nonpregnant women harbored monilial organisms.

TABLE I. STUDIES MADE DURING THE COURSE OF THIS INVESTIGATION ON THE INCIDENCE OF CANDIDA AND TRICHOMONAS IN PATIENTS WITH AND WITHOUT SYMPTOMS OF VAGINITIS OR DISCHARGE

	CLINIC	NUMBER OF PATIENTS EXAMINED	NUMBER OF PATIENTS HARBORING CANDIDA	NUMBER OF PATIENTS HARBORING TRICHOMONAS
Patients Without Symptoms of Vaginitis or Discharge.—	Maternity	162	49 (30.2%)	42 (25.9%)
	Gynecology	13	6 (46.0%)	7 (54.0%)
Patients With Symptoms of Vaginitis or Discharge.—	Maternity	72	44 (61.2%)	17 (23.6%)
	Gynecology	108	49 (45.4%)	41 (38.0%)

The usual array of factors predisposing to monilial vaginitis was present in this series of cases; 33 per cent were pregnant, 17 per cent had a history of recent systemic antibiotic therapy, 10.6 per cent had a family history of diabetes, and 4.3 per cent had had Trichomonas therapy. All patients were between 20 and 40 years of age, and no age appeared statistically to be particularly susceptible.

Laboratory Methods

Specimens of the discharge were obtained for mycologic study from each patient during the examination with the vaginal speculum. A portion was inoculated into Sabouraud's medium for culture. Another drop of discharge, mixed with 10 per cent potassium hydroxide, was examined for fungi directly under the microscope. At the same time a preparation mixed with normal saline was studied for Trichomonas.

The cultures in all but one case (one caused by *C. krusei*) revealed colonies which were grossly morphologically typical of *C. albicans*. The direct microscopic examination of material from the depths of such colonies revealed verticils of blastospores in profusion placed typically along pseudo-hyphae or true hyphae in the manner typical of *C. albicans*.

Cases exhibiting more than a minimum of Trichomonas organisms were not included in this study.

Method of Treatment

After preliminary trials with an effervescent tablet, a suppository, and a jelly containing the drug, a vanishing cream base containing 5 per cent Asterol dihydrochloride* was selected. Patients were instructed to apply this cream with a plunger-type vaginal applicator and subsequently to lie supine for one-half hour. This application was made before retiring for three successive nights; if no irritation was noted, the applications were increased to twice daily. Under these provisions about 50 per cent of the patients were able to use two applications a day; 45 per cent, once a day; and 5 per cent, less often.

Criteria of Cure

In a study of this type the criteria used to determine a "cure" are very important in evaluating the results. A patient was considered "cured" if she presented a normal vaginal vault on successive examinations over a period of one month while remaining asymptomatic during that time. Since the opinion of the patient was considered to be a useful factor in determining the cure, the appropriate designation is "clinical cure." Our observations parallel

*An experimental 5 per cent Asterol dihydrochloride vaginal cream, not generally available, was supplied by Hoffmann-La Roche, Inc., Nutley, N. J.

those of Hesseltine and Beckette[11] and Hart and Brown,[12] in that insisting on cultural negativity to establish a "cure" is not advisable. In this series as high a percentage of recurrences was sustained by those patients who did not harbor Candida after a "subjective cure" as by those who did. Patients who remained clear during the period of treatment, but had a recurrence of symptoms after therapy was stopped, were classed as "improved."

Since some women have a discharge during pregnancy which subsides spontaneously after delivery, patients beyond the sixth month of gestation were not included to avoid unjustly crediting the efficacy of the drug. Thus patients who began treatment during the early months of pregnancy and continued up to time of delivery without being cured were classed as treatment failures.

The vaginas of many of the successfully treated patients became free of Candida; in some cases, however, it was possible to demonstrate minimal numbers of the organism a week after the patient was symptom free. Subsequently, some of these patients became negative while others still harbored minimal numbers of the organisms without exhibiting symptoms. It seems that, in some cases without symptoms, a satisfactory compatible microbiologic balance which includes minimal amounts of Candida is re-established. In such a complex system, we cannot eliminate this possibility, recalling that many "normal" women persistently harbor the fungus.

Results of Treatment

Of the 65 patients studied, 54 (83.1 per cent) were "cured"; 4 (6.2 per cent) were improved; 7 (10.7 per cent) received no benefit. Pregnancy did not significantly influence these figures; of the 21 pregnant patients studied, 17 (81 per cent) were cured, 1 (4.8 per cent) was improved, and 3 (14.3 per cent) received no benefit; while in the 44 nonpregnant patients studied, 37 (84.1 per cent) were cured, 3 (7 per cent) were improved, and 4 (9.1 per cent) received no benefit. The length of time necessary to achieve a cure seemed to be similar in both groups.

Most of the 65 patients used Asterol for a period of two to four weeks and became completely asymptomatic in from two to three weeks. Many of the patients interviewed reported relief after the first or second application. It was necessary for four patients to use the cream for four weeks to obtain a cure and for two, as long as six weeks. Three patients in the group experienced relief during treatment but the symptoms recurred within a few days after therapy was stopped.

Of the 54 patients classified as "cured," 16 (29.6 per cent) sustained some degree of recurrence of vaginitis in from two to five months; this approximates the number who have had vaginitis due to various causes intermittently for years. Fifteen of the cured patients (27.7 per cent), after a follow-up of one month, failed to return for re-examination. Twenty-three patients (42.5 per cent) had no recurrence of symptoms two months or longer after the cessation of therapy. In those patients who sustained a recurrence, one was proved to be due to Trichomonas (after a lapse of three months without symptoms) and four were proved to be due again to Candida. In the remaining cases we did not have the opportunity to establish whether it was Candida or some other organism which caused the return of symptoms.

The Asterol cream produced some degree of irritation in 13 patients (20 per cent). In most of these it was present only following the first or second application of the cream but in 4 cases (6.2 per cent) the irritation was severe and the treatment was discontinued. These are included in the group of patients who failed to derive benefit from the treatment. A 2½ per cent Asterol vaginal cream is now being tried in such cases. All of the patients who stopped therapy because they developed irritation received relief of the discharge and itching during the time Asterol was being used. One patient who was not able to use the cream because of irritation obtained a cure with Asterol in the tablet form, indicating that, in this case, the vehicle and not the drug was the cause of irritation.

Comment

There is some question as to the advisability of continuing the medication after the symptoms have disappeared. It seems to be more satisfactory if the cream is used only for three or four nights after the disappearance of symptoms; thus we reduce the risk of altering too greatly the normal balance in the vaginal flora and, presumably, bring the patient to a state where she is able to establish her most compatible biologic system in a more natural and individualized manner.

Since several reports[7, 8, 9, 10] have indicated that toxic encephalopathy may result when Asterol is administered topically to children under 4½ years of age, the infants born to patients who used this drug intravaginally during pregnancy were observed and no evidence of toxicity was encountered.

Summary and Conclusions

1. Sixty-five patients who presented clinical evidence of vaginitis which was mycologically proved, exclusively or predominantly, to be due to Candida (moniliasis) were treated by intravaginal injection of a vanishing cream containing 5 per cent Asterol dihydrochloride once or twice daily.

2. Fifty-four patients (83.1 per cent) became asymptomatic and ceased to exhibit evidence of disease on physical examination within two to six weeks. These were classed as "subjective and clinical cures." Four patients (6.2 per cent) who obtained relief during therapy but sustained a recurrence of symptoms shortly after its cessation were classed as improved. Seven patients (10.7 per cent) were not benefited.

3. Sixteen patients (29.6 per cent) sustained a recurrence of vaginitis in from two to five months. This was due to Trichomonas in one case and Candida in four cases; the cause was not determined in the others.

4. Irritation was observed in 13 patients (20 per cent), severe enough to cause the discontinuance of therapy in 4 (6.2 per cent). Allergic sensitization was not encountered.

5. No toxicity was observed either in the patients or in the infants born to those who used the drug during pregnancy.

6. Asterol is a useful drug in vaginal moniliasis. Its value is enhanced by its freedom from objectionable color or odor.

References

1. Grunberg, E., Soo Hoo, G., Titsworth, E., Ressetar, D., and Schnitzer, R. J.: Tr. New York Acad. Sc. **13**: 22, 1950.
2. Reiss, F.: New York Acad. Sc. **13**: 28, 1950.
3. Stritzler, C., Fishman, I. M., and Laurens, S.: Arch. Dermat. & Syph. **63**: 606, 1951.
4. Ravits, H. G.: J. A. M. A. **148**: 1005, 1952.
5. Snyder, W.: Arch. Dermat. & Syph. **65**: 464, 1952.
6. Wilson, J. W., Levitt, H., and Plunkett, O. A.: J. Invest. Dermat. **19**: 319, 1952.
7. Wilson, J. W., Levitt, H., Harris, T. L., and Heiligman, E. M.: J. A. M. A. **150**: 1002, 1952.
8. Hitch, J. M.: J. A. M. A. **150**: 1004, 1952.
9. Featherston, W. M.: J. A. M. A. **150**: 1006, 1952.
10. Wallach, E. A.: Arch. Dermat. & Syph. **67**: 517, 1953.
11. Hesseltine, H. C., and Beckette, E. S.: Am. J. Obst. & Gynec. **58**: 553, 1949.
12. Hart, D. M., and Brown, C. H.: Brit. M. J. **2**: 813, 1952.

MEMBRANOUS DYSMENORRHEA: STUDIES IN ETIOLOGY AND TREATMENT

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THE term "membranous dysmenorrhea" refers to the painful passage of an endometrial cast of the uterus. This usually occurs some time during the first few days of menstruation. The endometrial cast is oftentimes referred to as a decidual cast because of the pronounced decidual reaction. Reference to this clinical entity has been very infrequent in the periodical literature. Because of the paucity of studies of this condition, it was felt that a report on the mechanism of the induction of decidual casts, as well as a review of our methods in the management of several patients with membranous dysmenorrhea, would serve as a further contribution to the understanding of this rather rare disorder.

As with dysmenorrhea, many theories have been proposed concerning the etiology of membranous dysmenorrhea. Mazer and Israel[1] stated that the cause was an increase in the production of estrogen and progesterone with incomplete disintegration of the resultant thickened endometrium. Larger portions of necrotic material stimulate a hypersensitive uterus reflexly in their passage and cause colicky contractions. The qualifying term "hypersensitive" was added because endometrial casts shed on other occasions are passed painlessly, leading to the conclusion that the physical passage per se is not the cause of the pain.[4] Cotte[2] also favored this theory. Curtis[3] felt that some cases were on an infectious basis, for he found minute microscopic abscesses and a pure culture of hemolytic streptococcus on several occasions. Davis[4] presented a review of the literature and noted that the premenstrual changes in the endometrium in these cases were similar to those of normal menstruation, except that the decidual reaction was exaggerated. He believed that the pain was similar to that of nonmembranous dysmenorrhea and was due to the same cause, i.e., excessive uterine motility and hypercontraction.

Wodon and Cordier[5] believed that the syndrome was due to normal but intense development of the spiral arterioles during the second part of endometrial growth and a period of regression of the functional layer. A phase of abnormally early and intense vasodilation was thought to occur and this was followed later by vasoconstriction of spiral arteries at their base. They

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concluded that Ergotrate and testosterone were the therapy of choice, the latter to prevent growth of the spiral arteries.

Recent contributions[6, 13] to the knowledge of uterine physiology suggest that the pain of dysmenorrhea may be caused by myometrial vascular spasm as a result of the release of menstrual toxin from a secretory endometrium. Anovulatory menses are painless, and it has been conjectured that this is because of the low toxin production from a proliferative endometrium. One is impressed by the invariable correlation of dysmenorrhea with a progestational type endometrium[7, 8, 9] or an ovulatory basal temperature curve.[10] The effectiveness of estrogen medication in the artificial production of anovulatory menses is thus explained. Because of the similarity of pain of membranous dysmenorrhea to that of primary dysmenorrhea, it was decided to treat some of our patients by the continuous suppression of ovulation by estrogen administration, and to treat others with androgens. Remarkable relief was obtained with the former method, and modification and improvement with the latter.

The following case studies deal with the experimental induction of membranous dysmenorrhea and with the management of several patients with this entity.

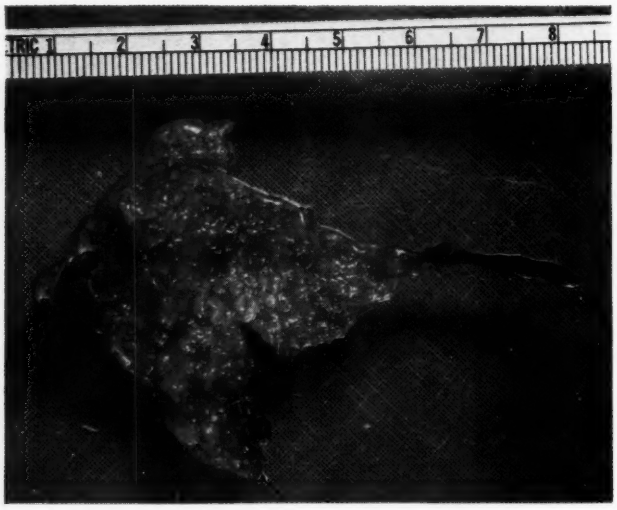


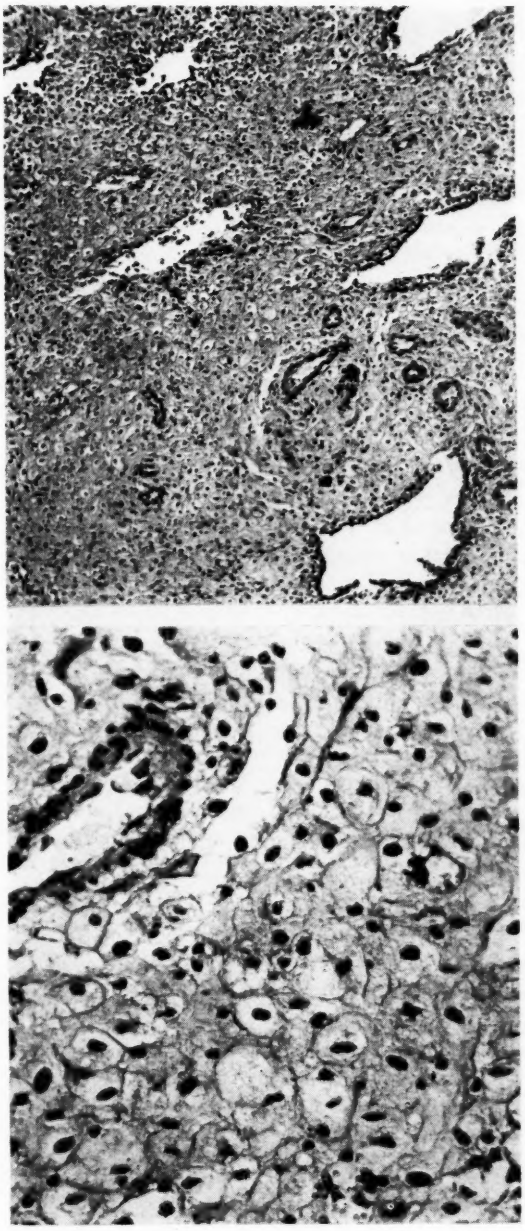
Fig. 1.—Gross specimen of cast, Case 1.

Accidental Induction of a Decidual Cast

CASE 1.—A white woman, aged 22 years, had been troubled with severe dysmenorrhea and hypermenorrhea since the menarche at the age of 13. Several dilations and curettages had been performed in the past with but temporary benefits. In January, 1953, the patient complained of prolonged, though mild, vaginal bleeding following estrogen therapy for dysmenorrhea. At this time she was found to have a severe hypochromic anemia (hemoglobin 6.5 Gm., red blood count 3,590,000, white blood count 5,950). Hematinics and transfusions were not very effective because of the continued loss of blood. It was decided to administer progesterone to arrest bleeding and thus induce a chemical curettage by the

withdrawal bleeding and concomitant endometrial shedding. An injection of 50 mg. of progesterone was given intramuscularly* once daily and bleeding was arrested within 24 hours. In lieu of the routine course usually followed in such cases, i.e., the administration

A.



B.

Fig. 2.—Histologic section of cast, Case 1. Note the marked decidual-cell reaction. (*A*, low power; *B*, high power).

*This was administered by the Hypospray. The cartridges of progesterone (25 mg. each) and the Hypospray used in this study were made available by E. R. Squibb & Sons.

of progesterone for five consecutive days, it was felt that it would be advantageous to postpone the withdrawal period for as long a time as possible by continuing the medication for an indefinite period. Consequently, this dosage of 50 mg. progesterone was administered daily, and raised to 75 mg. per day for a few days when breakthrough bleeding threatened. In this manner, bleeding was successfully withheld for thirty-one days. During this interval the blood picture rapidly improved (hemoglobin 12.5 Gm.) on iron and multivitamin therapy. On the thirty-second day, breakthrough bleeding occurred, with the passage of a well-formed endometrial (decidual) cast (Fig. 1) accompanied by severe pain. Medication was stopped. The withdrawal period lasted five days and was moderate in amount of flow. Histologic section of the cast showed hyperplastic secretory endometrium with pronounced stromal changes of a decidua-like type in a large membranous section of endometrium (Fig. 2). With corrective measures for the anemia and the administration of 25 mg. of progesterone intramuscularly per day for five to seven days before the anticipated menses for several months, the tendency to hypermenorrhea in this patient was brought under control. The patient has not been on any therapy for the past five months. The menstrual cycle has become stabilized, the amount of flow is normal, and the periods are without pain. No further endometrial casts have been passed.

CASE 2.—A white woman, 34 years of age, married ten years, complained of dysmenorrhea and sterility. She was on estrogen therapy when a phase of amenorrhea occurred. Her physician suspected that she might be pregnant. When spotting and mild bleeding occurred he thought that she was aborting and began the administration of 25 mg. progesterone intramuscularly daily. On the fifteenth day of progesterone administration, breakthrough bleeding occurred and the patient passed an endometrial cast with a great deal of pain. The tissue was sent to the senior author for examination and on histologic study proved to be a typical decidual cast. In retrospect, study of the patient's basal temperature record showed that there had been no ovulation. A pregnancy test, which had been performed prior to passing of the cast, was negative.

Comment.—Two young women with a history of dysmenorrhea were on estrogen therapy when abnormal bleeding occurred. The administration of prolonged and moderately large doses of progesterone intramuscularly was followed by the passage of an endometrial cast. It appears that the accidental production of decidual casts in these two instances implicates estrogen and progesterone in large amounts as the responsible factors or a contributing cause of membranous dysmenorrhea.

Acquired Membranous Dysmenorrhea in an Adult Woman

CASE 3.—Mrs. J. J., a 42-year-old married white woman, presented herself in April, 1949, with a chief complaint of severe dysmenorrhea and the passage of endometrial casts at each menses for a period of six months. For several months she had been treated by her physician with progesterone, and stated that the pain was aggravated by this form of treatment. She gave a history of two normal pregnancies and two miscarriages, the last miscarriage in September, 1948. Immediately after the last miscarriage, her menses became quite painful and casts were passed for the first time in her life. In addition, premenstrual tension and other symptoms appeared for the first time. The patient had had mild dysmenorrhea in 1947. Initial pelvic examination was normal.

In an attempt to suppress ovulation, estrogen therapy was instituted about the fifth day after passage of the cast in early April, 1949 (Fig. 3). Five milligrams of estradiol dipropionate was given by intramuscular injection and estrone sulfate, 2.5 mg. three times a day, was prescribed for the next nineteen to twenty days. The oral estrogen therapy was given more or less in this manner each month for the next four months, commencing about day 5 of each cycle. Anovulatory menses occurred after each course in April, May, and June, 1949, but in July bleeding failed to occur and, after a short delay, ovulation apparently set in and a menstrual period occurred early in August, accompanied by cast formation and moderate pain. Oral estrogens were again instituted commencing about

day 5 of each cycle for the next few months with results similar to those obtained during the first three months, i.e., anovulatory painless menses without cast formation. Then, in November, 1949, it was decided to give estrone sulfate in doses of 2.5 mg. daily uninterruptedly, and to induce bleeding at regular intervals by superimposing the oral administration of anhydrohydroxyprogesterone, 10 mg. twice a day, for five consecutive days. This regimen was followed for five months with excellent results. All medication was discontinued one year after start of therapy. Basal temperature charts revealed anovulatory cycles, except for August, 1949, until May and June, 1950 (Fig. 4). In May, 1950, an ovulatory menstrual period occurred, without cast formation or pain, and in June, 1950, 10 mg. anhydrohydroxyprogesterone was given during the last ten days of the ovulatory cycle for premenstrual tension. Cyclic anhydrohydroxyprogesterone and ammonium chloride were continued for the next six months for ten days prior to each menses. From June, 1950, to April, 1951, the patient passed an endometrial cast each month without pain. Because, at this time, she began to experience some hypermenorrhea, a hematinic was prescribed and two pellets of testosterone were implanted subcutaneously in May, 1951. Following this procedure, menses occurred regularly and normally. At the present writing, more than four and one-half years after the start of the original therapy, the patient remains well, the intervals between menses have increased, the flow is normal in amount, and there has been no cast formation or dysmenorrhea.

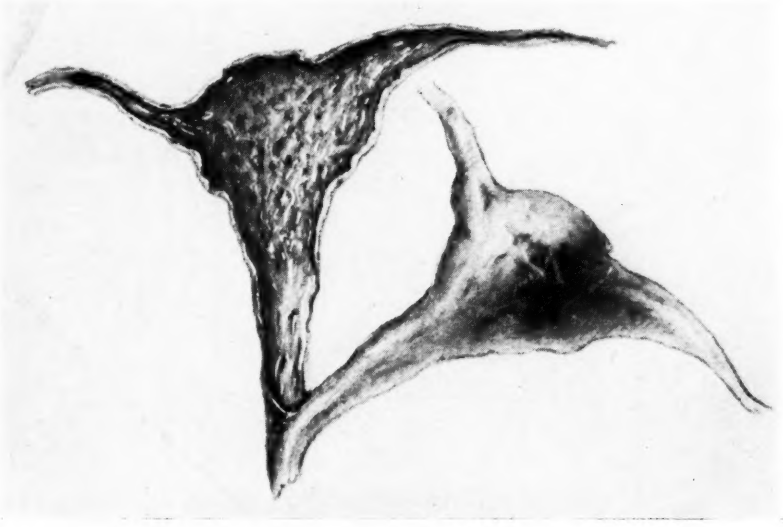


Fig. 3.—Drawing of cast passed by patient described in Case 3.

Membranous Dysmenorrhea in a Young Girl

CASE 4.—Miss B., a 21-year-old white unmarried woman, first presented herself in July, 1952, with the chief complaint of passing an endometrial cast each month for the previous five or six years, each time with very severe pain. She gave a history of onset of menses at the age of 14 years. Periods had occurred regularly every 28 days and were of five to six days' duration. A dilation and curettage had been performed by her physician but afforded no relief from the membranous dysmenorrhea and each month she required codeine for the severe pain. Pelvic examination revealed a third-degree retroversion of the uterus.

In view of the experience gained in the management of Case 3, it was decided to suppress ovulation by the continuous administration of estrogens, superimposing each month anhydrohydroxyprogesterone, 10 mg. three times a day for five consecutive days,

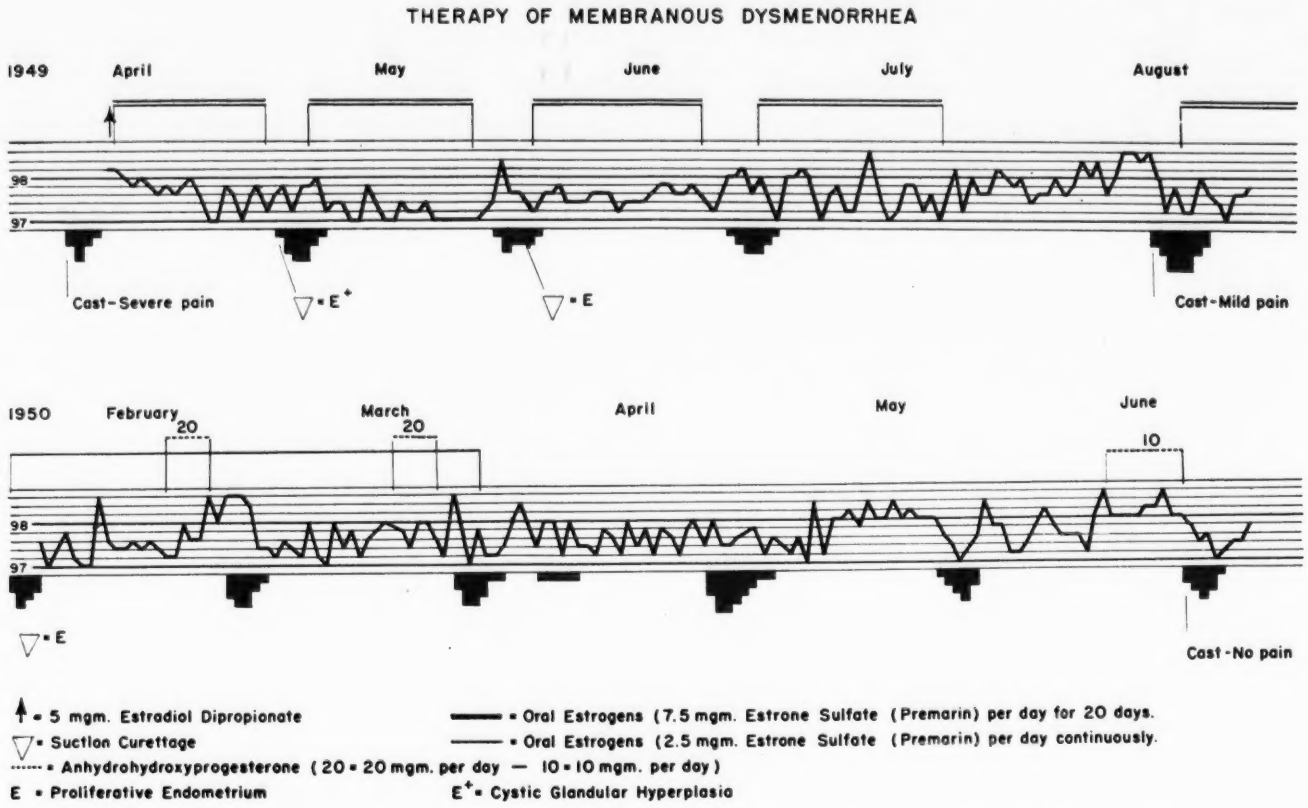


Fig. 4.—Therapy of membranous dysmenorrhea in a white woman 42 years of age, gravida iv, para ii. In an attempt to suppress ovulation, estrogen therapy was instituted about the fifth day after passage of the cast in early April, 1949. Five milligrams of estradiol dipropionate was given by intramuscular injection and estrone sulfate, 2.5 mg. three times a day, was prescribed for the next nineteen to twenty days. The oral estrogen therapy was given more or less in this manner each month for the next four months, commencing about day 5 of each cycle. Anovulatory menses occurred after each course in April, May, and June, 1949, but in July bleeding failed to occur and, after a short delay, ovulation apparently set in and a menstrual period occurred early in August accompanied by cast formation and moderate pain. Oral estrogens were again instituted commencing about day 5 of each cycle for the next few months with results similar to those obtained during the first three months, i.e., anovulatory painless menses without cast formation. Then, in November, 1949, it was decided to give estrone sulfate in doses of 2.5 mg. daily uninterruptedly, and to induce bleeding at regular intervals by superimposing the oral administration of anhydrohydroxyprogesterone, 10 mg. twice a day for five consecutive days. This regimen was followed for five months with excellent results. All medication was discontinued one year after start of therapy. Basal temperature charts revealed anovulatory cycles, except in August, 1949, until May and June, 1950. From June, 1950, to April, 1951, the patient passed an endometrial cast each month without pain.

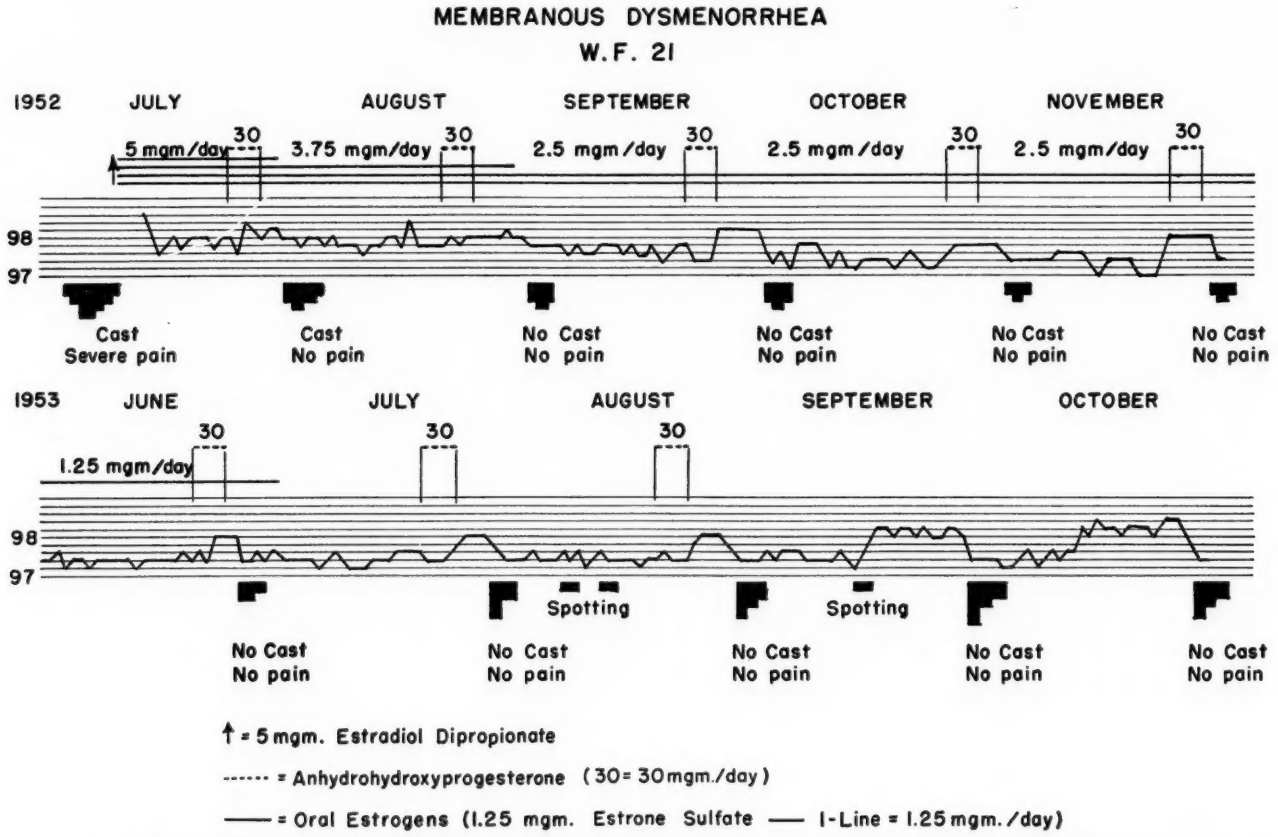


Fig. 5.—Treatment of membranous dysmenorrhea in a white woman 21 years of age. Ovulation was suppressed by the continuous administration of estrogens. On the eighth day of the cycle in July, 1952, she was given an intramuscular dose of 5 mg. estradiol dipropionate and was immediately placed on estrone sulfate, 1.25 mg. four times a day for one month, three times a day for the second month, twice a day for the next seven months; then the dose was reduced to 1.25 mg. once per day for the remaining three months of therapy (April to June, 1953). All estrogen therapy was discontinued on July 1, 1953, about one year after the start of therapy. Anhydrohydroxyprogesterone, 10 mg. three times a day for five consecutive days, was superimposed each month at regular intervals to induce a withdrawal period and thus avoid excessive bleeding as a result of the continuous estrogen therapy. Anhydrohydroxyprogesterone was continued at monthly intervals for two months afterward in order to avoid excessive estrogen withdrawal bleeding. Basal temperature records were kept during the therapy and all cycles appeared to be anovulatory in type. The elevation of temperature near the end of each cycle coincided with the progestin therapy. After the first month of treatment an endometrial cast was passed without pain. All subsequent menses were scant in amount of flow and free from pain, and no endometrial casts were passed after August, 1952. At this time the patient is experiencing normal cyclic menstruation without pain or cast formation.

five to seven days prior to the time of the anticipated menses, in order to avoid any excessive bleeding or spotting. On the eighth day of the cycle in July, 1952, she was given an intramuscular dose of 5 mg. estradiol dipropionate and was immediately placed on estrone sulfate, 1.25 mg. four times a day for one month, three times a day for the second month, twice a day for the next seven months; then the dose was reduced to 1.25 mg. once per day for the remaining three months of therapy (April to June, 1953). All estrogen therapy was discontinued on July 1, 1953, about one year after the start of therapy. Anhydrohydroxyprogesterone was continued at monthly intervals for two months afterward in order to avoid excessive estrogen-withdrawal bleeding. Basal temperature records were kept during the therapy and all cycles appeared to be anovulatory in type. The elevation of temperature near the end of each cycle coincided with the progestin therapy. After the first month of treatment she passed an endometrial cast with no pain. All subsequent menses were scant in amount of flow and free from pain, and she passed no endometrial casts after August, 1952. At the time of this writing (November, 1953), the patient is menstruating regularly, with a normal amount of flow and without pain or cast formation (Fig. 5).

Androgen Therapy

Cases 5, 6, and 7 were patients 20, 33, and 35 years of age, respectively, who passed membranous casts of the uterus with each menses with severe pain. Each of these patients was being studied for sterility. Continuous suppression of ovulation seemed contraindicated since the purpose was not to interfere with ovulation and the opportunity for conception. Case 5 received two pellets of testosterone on two different occasions six months apart. Relief was obtained in each instance for 3 to 4 months. Conception followed and the patient carried uneventfully to term. In Case 6, three pellets of testosterone were implanted. Voice changes and some hirsutism resulted and although the patient experienced relief of pain for three or four months before cast formation recurred, further therapy with androgens was considered undesirable because of the masculinizing stigmas. Case 7 received three pellets of testosterone. Partial relief for five or six months was obtained. Instead of the passage of a single cast with severe pain, there now occurred the passage of several small fragments of endometrial tissue (partial casts) with marked reduction in pain.

Comment

The similarity of results obtained in Cases 3 and 4 of membranous dysmenorrhea reported here, and the results of estrogenic therapy in primary dysmenorrhea prompt one to draw an analogy between the two conditions. It is probable that Davis[4] was correct in his assumption of identity. It is well known that progesterone induces a decidual reaction of the uterus and this is corroborated by our observations in the accidental production of casts in two instances (Cases 1 and 2). Thus one may postulate that membranous dysmenorrhea represents a hyperprogestational response. Progesterone has been found to increase the severity of membranous dysmenorrhea and is contraindicated in its treatment. The suppression of ovulation and the prevention, in this manner, of the formation of progestational or secretory endometrium is, therefore, rational therapy.[11] Williams[12] also recommends this form of therapy. In some manner, not at present understood, androgen therapy is capable of so modifying progesterone activity that it may be used to some advantage in therapy of this condition, as the results in our Cases 5, 6, and 7 indicate. However, it is not always feasible to use androgen therapy. This is particularly true in the cases of young unmarried girls and in women who are already

moderately hirsute. How and why prolonged estrogen therapy modifies uterine responsiveness so that, after cessation of therapy, resumption of cyclic menstruation with cast formation may occur but *without* pain, is not at present completely explicable.

The relationship of this syndrome to the formation of menstrual toxin as described by the Smiths[13] offers interesting theoretical possibilities. If the pain of dysmenorrhea were due to myometrial vascular spasm, then the severity of the pain in this condition and the shedding of an endometrial cast (rather than the minute fragments of endometrium seen in a normal period) might be due to the intensity of vascular spasm in the myometrium and the endometrium. The cast formation might be the result of severe vasospasm, widespread simultaneous necrosis, and uniform sloughing. As to the cause of this hypersensitive vascular response, one might theorize that it could be due to quantitative increase of qualitative change in the toxin as a hyperprogestational effect.

Summary

1. A patient receiving daily doses of 50 to 75 mg. of progesterone intramuscularly for 31 consecutive days passed an endometrial cast of the uterus. Another patient receiving daily doses of 25 mg. of progesterone passed a cast on the fifteenth day with severe pain. The accidental induction of a decidual cast in this manner lends support to the theory that membranous dysmenorrhea represents a hyperprogestational response.

2. A new approach to the management of patients with membranous dysmenorrhea by the continuous suppression of ovulation for a period of one year is presented. This method proved most efficacious in two patients and was accomplished by administering oral estrone sulfate continuously and interposing small doses of anhydrohydroxyprogesterone for five days at monthly intervals to induce withdrawal periods.

3. Androgen therapy (in the form of pellet implantation), though not as efficacious as estrogen therapy, nonetheless proved temporarily effective in management of three patients with membranous dysmenorrhea.

4. Uterine physiology may be so modified by therapy that passage of a membranous cast may occur without pain.

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References

1. Mazer, C., and Israel, S. L.: Diagnosis and Treatment of Menstrual Disorders and Sterility, New York, 1951, Paul B. Hoeber, Inc.
2. Cotte, G.: Presse méd. **37**: 1542, 1929.
3. Curtis, A.: Textbook of Gynecology, Philadelphia, 1940, W. B. Saunders Company.
4. Davis, Albert A.: Dysmenorrhoea: Its Aetiology, Pathology and Treatment, New York, 1938, Oxford University Press.
5. Wodon, J., and Cordier, R.: Bruxelles-méd. **28**: 1627, 1948.

6. Greenblatt, R. B., Barfield, W. E., and Hammond, D.: Am. J. Obst. & Gynec. **61**: 565, 1951.
7. Wilson, L., and Kurzrok, R.: Endocrinology **23**: 79, 1938.
8. Sturgis, S. H., and Albright, F.: Endocrinology **26**: 68, 1940.
9. Greenblatt, R. B., McCall, E., and Torpin, R.: Am. J. Obst. & Gynec. **42**: 50, 1941.
10. Lyon, R. A.: Surg., Gynec. & Obst. **76**: 729, 1943.
11. Greenblatt, R. B.: Office Endocrinology, ed. 4, Springfield, Ill., 1952, Charles C Thomas.
12. Williams, R. H.: Textbook of Endocrinology, Philadelphia, 1950, W. B. Saunders Company.
13. Smith, G. V., and Smith, O. W.: Am. J. Obst. & Gynec. **54**: 201, 1947.

CIRSOID ANEURYSM OF THE UTERUS

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THE purpose of this paper is to bring attention to a rarely observed lesion. Only 5 cases of cirsoid aneurysm of the uterus have been previously reported. Dubreuil and Loubat[1] of France reported the first case in 1926. Their article prompted Graves and Smith[2] of this country to report another case in 1927. Since discovery and treatment in 1949 of the case herein described, 3 additional cases[3, 4, 5] have been discovered and reported in the American literature.

Case Report

D. G., a white woman, aged 43 years, a nulligravida, was first seen on Jan. 14, 1949, for severe menorrhagia. Her menses had begun at the age of 12, had recurred regularly every twenty-six to twenty-eight days until two years previously, after which the interval increased to thirty-five to forty-two days. The duration of flow had always been five to seven days. There was no history of intermenstrual bleeding. Throughout the patient's menstrual life the flow had been very excessive. She had virtually lived by the calendar, always being in fear of sudden "embarrassment." Her mother had made special, extra heavy pads for her during childhood. Since sufficient protection was almost impossible, rubber pants were sometimes worn as a precaution.

Although various and sundry medical therapy for the purpose of "regulating the flow" had been tried throughout her menstrual life, nothing seemed to influence the profuse, clotting, and gushing periods. The patient had for many years remained continuously under the care of internists, during which time vitamins, liver, and iron were prescribed in wholesale lots for her anemia and poor health.

In 1935, the patient consulted a gynecologist who told her that the uterus was the size of a two months' pregnancy and very soft. She was again seen in 1944 independently by two gynecologists, one of whom made a diagnosis of fibromyomas. In 1945, an unusually excessive period necessitated a blood tranfusion, but again, no surgical treatment was given. On Jan. 5, 1949, on the second day of a regular menstrual period, a massive hemorrhage occurred which within fifteen minutes left her in a "weakened condition."

The patient's past history included appendectomy, 1928; hemorrhoidectomy, 1948, followed by one transfusion. There was no history of serious medical illness, no history of accident or other trauma, no curettements, and no pregnancies. The patient had always been chronically underweight, anorexic, anemic, fatigued, and had poor resistance to ordinary infections. Intolerance to cold weather was her reason for having moved to Texas.

Physical Examination.—Although the patient was 5 feet, 2 inches tall, her weight was only 87 pounds. Pallor was marked. The lungs were clear. There were no murmurs. The blood pressure was 110/60 and the pulse 88. A medical consultant was unable to demonstrate abnormal cardiovascular signs. The lower extremities showed no edema or varicosities, and they were of equal temperature.

The external genitals were normal. The cervix was slightly enlarged, but healthy in appearance. The positive findings consisted of marked pulsations in the parametrial areas, with a continuous palpable thrill which was accentuated by each heartbeat. These pulsations were similar to those palpable in advanced pregnancy. The same thrill was present to some degree over the entire uterus, which was the size of a seven to eight weeks' pregnancy and very soft. Its contour did not seem abnormal. No adnexal masses were palpable. Auscultation and direct ear application over the lower abdomen revealed a loud continuous bruit with systolic accentuations. The bruit was comparable to a uterine souffle heard in advanced pregnancy. Cystoscopic examination showed no abnormalities within the bladder.

Fig. 1.—Gross section of myometrium showing numerous vessels of all sizes. Tortuosity of large vessel demonstrated. Note eversion of cut vessel wall.

A. *B.*

Fig. 2.—Gross section of myometrium showing the two sides of a 5 mm. thick segment of uterus. *A*, Uterine vessels immediately after entering myometrium. *B*, Same vessels after communicating to form a single larger vessel or sinus. Fig. 1 shows the same vessel at a higher level.

Laboratory.—When first seen on Jan. 14, 1949, which was nine days following the last acute hemorrhage, the red cell count was 3.02 million and the hemoglobin 7.95 Gm. per cent. Ten days later and without transfusion, the red cell count had increased to 3.69 million and

the hemoglobin to 10.2 Gm. per cent. The white cell count and differential were normal; urine, negative; bleeding time, one minute; coagulation time, four minutes. A uterogram, using Lipiodol, showed the uterine cavity to be normal in size and contour.

Treatment.—A clinical diagnosis of arteriovenous aneurysm, most likely of the uterus, was made. The patient was admitted to Hermann Hospital, Jan. 25, 1949. At operation on Jan. 27, 1949, the uterus was found to be roughly the size of a two months' pregnancy. It was moderately cyanotic and extremely boggy. By manual compression the total bulk

Fig. 3.

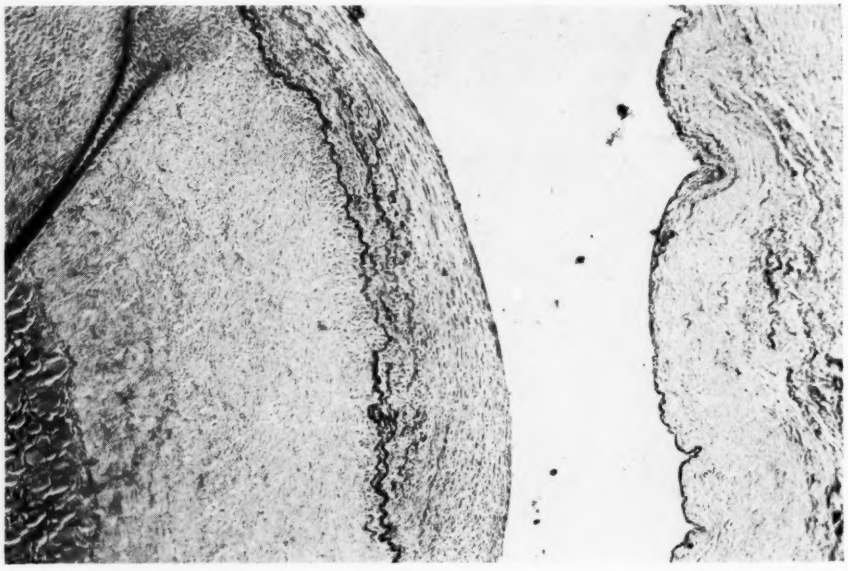
Fig. 4.

Fig. 3.—Small vessel showing a dense internal elastic membrane typical of an artery. (Masson trichrome stain.)

Fig. 4.—Venous component. Internal elastic membrane practically absent. Thin muscle wall contains fibrous tissue. (Masson trichrome stain.)

of the uterus could be reduced by one-half. It would immediately re-expand after the release of pressure. This compressibility was especially marked in the upper part of the body and the fundus. The uterus was visibly pulsating and this pulsation was even more evident by palpation. Abnormally distended, tortuous, and slightly pulsating blood vessels were present in the upper part of the broad ligaments, over the bladder, and one moderate-sized vessel passed into each round ligament. The left ovary contained a chocolate cyst, to which the left tube was adherent. Several pathognomonic lesions of endometriosis were present in the cul-de-sac and in the vesicouterine reflection. Preliminary preparations had been made for taking colored movies, in anticipation of an unusual lesion.

Surgery consisted of total hysterectomy and removal of both tubes and ovaries. Blood loss was minimal, but the necessity of careful hemostasis was evident. Five hundred cubic centimeters of blood was given on the day of surgery, and 500 c.c. on the second postoperative day. The patient was dismissed from the hospital on the eighth day. One



A. Arterial. *B. Venous.*

Fig. 5.—Large sinus or vessel showing characteristics of both artery and vein in a single low-power field (vessel collapsed). Typical arterial characteristics on left, with thick internal elastic membrane and thick muscular media. On the right, indistinct internal elastic layer and a thin muscular layer.

month later the hemoglobin was 12 Gm. per cent. The patient was last seen April 15, 1952, when the hemoglobin was 14 Gm. per cent and her weight 104 pounds. Her good health and energy were in contrast to her chronic debility before surgery.

Gross Pathology.—The specimen consisted of a soft, slightly globular, intact uterus and cervix measuring 11 by 7 by 5 cm. The tubes and ovaries were attached. The serosal surface was smooth. The myometrium measured from 14 to 27 mm. in thickness. The endometrium was smooth and of average thickness. Coursing through all areas of the myometrium and in all directions were numerous blood vessels of all diameters up to 1 cm. (Fig. 1). The largest vessel seen traversed transversely the myometrium of the fundus. It was possible to trace this vessel to the right where it joined two large vessels, presumably the uterine artery and vein (Fig. 2). The two large vessels were the largest ones traversing the right parametrium and before entering the myometrium they occupied the usual location of the uterine vessels. The two vessels united after entering the myometrium at a level slightly below the round ligament. This was the point of origin of the

larger vessel or sinus. All vessels in the myometrium were tortuous and difficult to trace for more than a few millimeters. Grossly, the vessels had walls of varying thickness and in the fixed specimen many everted to give the cut section of the myometrium a punctate appearance (Fig. 1). The uterine vessels on each side of the uterus were large and tortuous, being several times greater in diameter than the average uterine vessel. In the fresh specimen several of the smaller vessels in the myometrium were seen to approach the endometrium. The tubes and ovaries were not remarkable except for a chocolate cyst in the left ovary to which the tube was adherent.

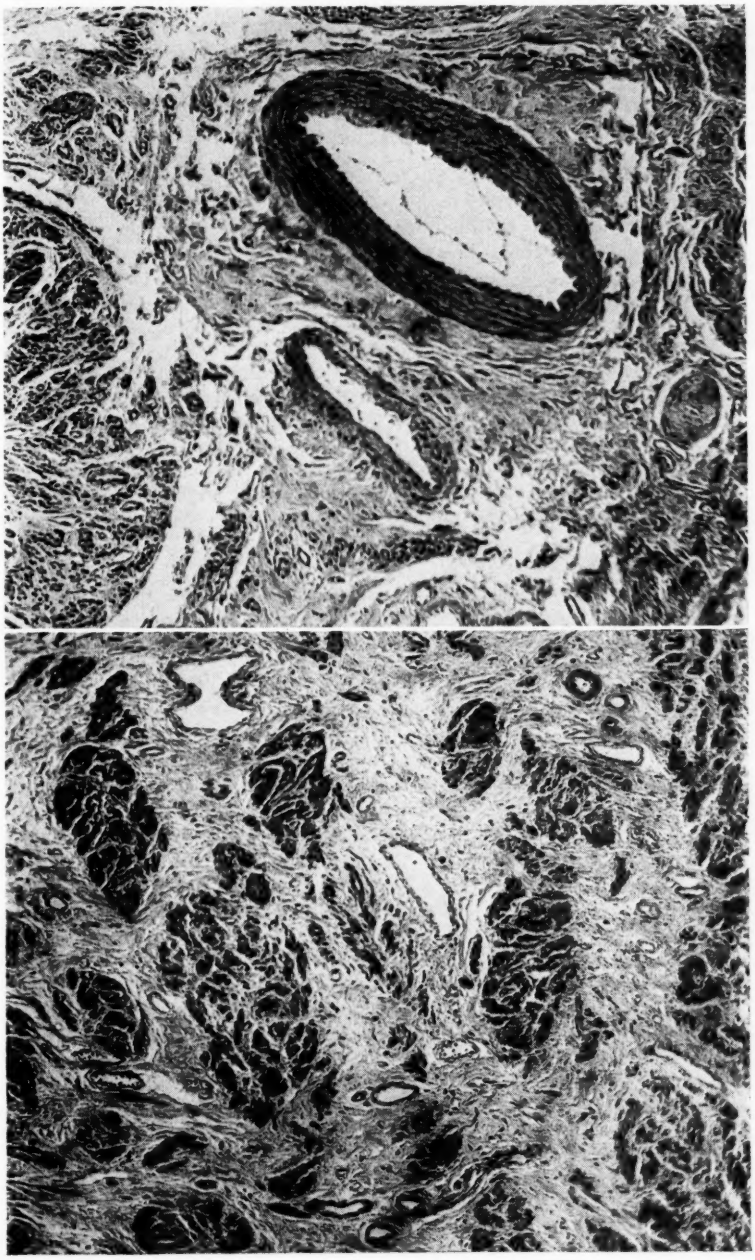


Fig. 6.—Myometrium showing marked fibrosis, especially about blood vessels. Darkly stained tissue represents myometrium, and light staining, fibrous tissue.

Microscopic Pathology.—Almost every microscopic field throughout the myometrium showed an abnormal number of blood vessels. These vessels varied from a fraction of a millimeter to 1 cm. in diameter. Some showed typical characteristics of arteries (Fig. 3) mainly as indicated by a dense internal elastic membrane and a thick muscular wall, while others were typically venous (Fig. 4). Many of the vessels could not be classified into distinct artery or vein, either the histologic appearance being indefinite or single vessels showing the characteristics of each. Thick intimal plaques were common. The intima, especially of the veins, was frequently frayed (Fig. 4). Many of the larger vessels showed abrupt changes in the character of the component layers. The muscular media was especially variable in thickness, direction of fibers, and percentage of fibrous tissue. The internal elastic membrane in a single field might vary from marked thickness to loss of distinction. One section through the large sinus or vessel (described under Gross, Fig. 2, *B*) shows it to have characteristics of both artery and vein. The characteristics of each could be seen in a single low-power field (Fig. 5). The vessel wall on one side showed a dense internal elastic membrane and a thick muscular media, while the opposite wall had little or no internal elastic layer and a thin muscle layer with the bundles separated by distinct fibrous connective tissue. The two large uterine vessels (Fig. 2, *A*) proximal to this large sinus or vessel resembled each other histologically and were mainly arterial in character. In spite of their histological similarity it must be assumed that they originally represented uterine artery and uterine vein. Since the two vessels were proximal to the large sinus into which they merged, they could not be considered branches or tributaries of the larger vessel.

The myometrium (Fig. 6) showed a marked diffuse interstitial increase in fibrous tissue. The fibrous tissue comprised more than 50 per cent of the substance of the wall in most fields, almost completely replacing it in other fields. Fibrosis was especially marked near blood vessels.

The endometrium was in a proliferative phase, the glands being rather straight and the stroma relatively dense. The endometrium did not appear abnormal. Microscopic examination of the tubes and ovaries revealed nothing unusual.

Comment

I can add very little to the excellent comments made by the five previous authors reporting on the condition. In view of the classical signs of uterine aneurysm in the case herein reported it would have been difficult to escape a suspicion of its presence. To my satisfaction a direct and major arteriovenous communication was demonstrated, and, in view of other evidence presented, the presence of multiple arteriovenous communications must be assumed. After considerable library investigation[6-11] and after detailed study of this case, some definite opinions have been formulated.

Etiology.—It seems probable that the lesion is congenital in origin. Sabin[6] has shown that arteries and veins arise from a common embryonic capillary bed. She has further shown that vessels in early development may carry arterial or venous blood in one direction to carry subsequently the opposite kind of blood and with a reversal in the direction of flow. These basic facts appear to afford an explanation of how a failure of differentiation into the definitive components of the vascular system could result in multiple abnormal communications within a single viscus or any isolated area of the body.

That physiologic or normal arteriovenous anastomoses exist has been demonstrated in various animals, including man, and in various tissues. It would thus also seem understandable how these normal "derivating channels"

could easily develop into pathologic arteriovenous anastomoses. It seems even more difficult to understand why abnormal anastomoses do not develop with greater frequency.

The indistinct and variable characteristics of the components of the lesion with the resulting difficulty of classifying into arterial or venous are partially explained by the work of Reid[11] who showed that there can occur arterialization of veins involved in aneurysms. There can be little doubt that the histologic appearance of vessels can develop or change according to the function imposed. Sabin's work[6] on embryonic development of vessels further supports this view. The variable stresses and strains which must occur within the lumina of involved vessels explain why an individual vessel can show the characteristics of artery and vein within a single microscopic field. Four of the five previous authors reporting have specifically mentioned the difficulty of classifying the component vessels.

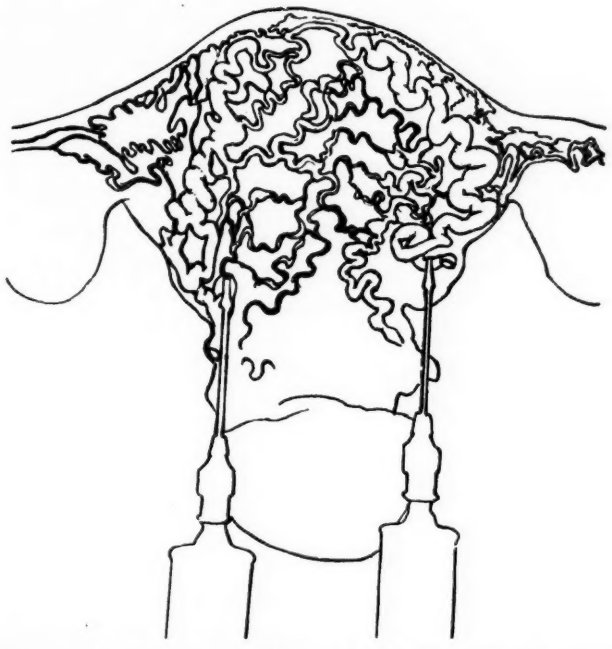


Fig. 7.—Tracing made from x-ray picture which was too thin for reproduction.

The features of the case being presented offer additional evidence in favor of the congenital nature of the lesion. The probability of trauma could be practically eliminated since the patient had never been pregnant, and since the uterus had never been instrumented. Also of importance is the fact that the patient had experienced gushing menorrhagia since the menarche, permitting the assumption that the anomaly had been present before puberty.

Classification.—Although the five cases previously reported appear to be fundamentally the same pathological process, the authors have chosen four different terminologies for reporting them: "Cirsoid Aneurysm,"[1-2] "Arteriovenous Aneurysm of Uterine Artery and Vein,"[3] "Arteriectasia of the Uterine

Artery,''[4] and ''Uterine Arteriovenous Fistula.''[5] With the possible exception of Berlin and Horwitz,[4] all authors suggested that their cases represented abnormal arteriovenous communications. The terms arteriovenous aneurysm and arteriovenous fistula are not only all embracing, but as a rule imply a single abnormal communication between trunk-line vessels. The over-all gross and microscopic appearance of the case being presented strongly suggests multiple abnormal communications between arteries and veins. Further evidence of multiple direct communications is the tracing from the x-ray picture (Fig. 7) of the removed specimen after 20 c.c. of Lipiodol had been injected into the vascular system through the left uterine vessels. The Lipiodol, a relatively thick substance, passed freely from the left side to the right side of the uterus and relatively large vessels could be seen traversing the transverse diameter without evidence of intervening capillary beds.

The lesion could be included under a number of classifications, but this only affirms the existing confusion as regards the classification of vascular anomalies of this nature. Definitely the term ''cirsoid aneurysm'' is not clearly defined in the literature. Being unconvinced of a better classification and desirous of seeing the lesion reported under a single heading, I shall call the case herein reported ''Cirsoid Aneurysm,'' in agreement with the original authors[1-2] reporting on the condition. Moore[12] states, ''multiple arteriovenous aneurysms with the formation of a mass of dilated arteries and veins constitute the cirsoid aneurysm'' and Meleney[13] defined cirsoid aneurysm as ''a pulsating tumor caused by an anastomosis between the small arteries and veins, without the interposition of capillaries.''

Diagnosis and Treatment.—The classical cirsoid aneurysm of the uterus should show the majority of the following signs and symptoms:

1. Menorrhagia or metrorrhagia, severe,
2. Uterine enlargement, softness, and compressibility,
3. Palpable thrill,
4. Audible bruit,
5. Parametrial pulsations in a nonpregnant uterus.

The treatment after the appearance of symptoms is complete hysterectomy. Removal of the tubes and ovaries should be according to indications. Bothersome bleeding at the time of operation has been commented on by previous authors, but its control should be fairly simple if the necessity of careful hemostasis is recognized. Four of the 5 cases previously reported had curettements and in each instance serious bleeding resulted from the procedure. The case being presented had no preliminary dilatation and curettage for fear of this complication. If the lesion is suspected, and a dilatation and curettage is to be done, a good supply of blood should be immediately available, and the operating team should be in readiness. Cirsoid aneurysm should be easily recognized if its existence is borne in mind and if several of the previously mentioned signs and symptoms are present.

Addendum.—Since this report was submitted for publication a similar case has been reported under the title of "Arteriovenous Aneurysm of the Uterus."[14]

References

1. Dubreuil, G., and Loubat, E.: Ann. d'anat. path. **3:** 697, 1926.
2. Graves, W. P., and Smith, G. Van S.: AM. J. OBST. & GYNEC. **14:** 30, 1927.
3. Reynolds, R. P., Owen, C. I., and Cantor, M. O.: J. A. M. A. **141:** 841, 1949.
4. Berlin, P. F., and Horwitz, D.: AM. J. OBST. & GYNEC. **64:** 347, 1952.
5. Gaines, J. A., and Greenwald, J. C.: AM. J. OBST. & GYNEC. **65:** 997, 1953.
6. Sabin, F. R.: Contrib. Embryol. Carnegie Inst. **14:** 139, 1922.
7. Reid, M. R.: Arch. Surg. **10:** 996, 1925.
8. Seeger, S. J.: Surgery **3:** 264, 1938.
9. Thompson, A. W., and Shafer, J. C.: J. A. M. A. **145:** 869, 1951.
10. Holmon, E.: Arteriovenous Aneurysm: The Macmillan Surg. Monograph, New York, 1937, The Macmillan Company.
11. Reid, M. R.: Bull. Johns Hopkins Hosp. **21:** 43, 1920.
12. Moore, Robert A.: Textbook of Pathology, Philadelphia, 1944, W. B. Saunders Company.
13. Meleney, F. L.: Surg., Gynec. & Obst. **36:** 547, 1923.
14. Williams, G. A.: AM. J. OBST. & GYNEC. **67:** 198, 1954.

HAZARDS IN THE INTRAVAGINAL USE OF POTASSIUM PERMANGANATE

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THE apparent increase in the use of and the complications resulting from potassium permanganate tablets and douches in the vagina has prompted this report. It is hoped that its use in gynecologic disorders can be further discouraged.

Potassium permanganate has been used for many years and for many reasons in the various specialties, particularly dermatology, urology, gynecology, surgery, and internal medicine. Although many uses are now obsolete, in dermatology it has been prescribed chiefly for the dermatomycoses, in urology for urethral and bladder irrigations, in gynecology as a douche in the treatment of infections of the vagina and pelvic organs, in surgery as a preoperative skin disinfectant, and in medicine as an antidote for certain ingested organic poisons.

Pharmacologically its action is that of an oxidizing agent. When it comes in contact with organic material it is reduced to manganese dioxide with the liberation of nascent oxygen. Its action in very dilute solutions is superficially irritating, but further injury may take place, especially in higher concentrations, due to the formation of potassium hydroxide which will penetrate into deeper tissues. This reaction is presented in the following equation:

$$4\ KMnO_4 + 2\ H_2O \rightarrow 4KOH + 4\ MnO_2 + 3\ O_2.$$

Smooth muscle is stimulated by direct contact with 0.2 to 1 per cent solutions. The excised uterus of a guinea pig shows prolonged tonus when placed in potassium permanganate solution; this is relieved by epinephrine but not by atropine. Oral administration in rabbits of a 1 to 2 per cent solution increases uterine activity and daily oral administration causes death of the embryos in pregnant guinea pigs and abortion in pregnant mice. It is absorbed to a slight degree from the alimentary canal and is deposited mainly in the liver and kidneys. It also passes through the placenta to the fetus. Excretion is mainly by the intestinal tract and in the bile but significant amounts are also found in the urine.

Its toxicity when ingested may manifest itself either mildly as an acute gastroenteritis or severely as circulatory collapse secondary to local injury and hemorrhage. Jetter and Hunter have shown that it may also be a systemic poison acting as an acute hemolytic agent with the production of methemo-

globinemia and the formation of pigment casts in the kidney tubules. Hyperpotassemia is another toxic complication; the source of this excess is by direct absorption and/or release of potassium from hemolysis of red blood cells. The parenteral administration of manganese dioxide leads to convulsive seizures and terminal coma in animals, but fortunately manganese dioxide is highly insoluble and absorption would be unlikely. Chronic toxicity leads to changes in the basal ganglia and produces symptoms simulating Parkinson's syndrome.

The use of potassium permanganate in surgery as a preoperative skin preparation has become obsolete, as has its use in poisoning by alkaloids. Kautz states that the presence of food in the stomach and the markedly irritant actions have limited its use as an antidote for accidentally ingested poisons. Urologists no longer consider it adequate as a urethral irrigant. Krantz has said that its irritation and the production of better sources of nascent oxygen have in a large measure made its use outmoded. It is still recommended, however, in the treatment of dermatomycoses, eczema, and other skin lesions. Trussell's book on *Trichomonas vaginalis* lists more than 175 different treatments, one of which is potassium permanganate douches, but his comment that it has been found inadequate agrees with the recent clinical experience of others. Potassium permanganate douches have also been used and found ineffective in the treatment of fungus vaginitis. Any possible therapeutic benefit from this type of warm douche on pelvic inflammatory disease would be ascribed to the heat and not to the agent. In the past it was seldom recommended in concentrations greater than 1:5,000 and even at that dilution was markedly irritant.

Within the last twenty years and through devious channels of information, potassium permanganate tablets inserted into the vagina and potassium permanganate solutions as douches have been recommended as abortifacients. The incidence of this practice has apparently been on the increase. Apparently the use spread to this country from Europe where reports attesting the popularity of potassium permanganate as an abortifacient first appeared in the nineteen thirties, chiefly in the Italian and French literature. Later reports appeared from South America. The first report in the American journals was by Shull in 1941. He noted 17 cases which demonstrated the complications arising from use of the agent seen in the Boston area between 1936 and 1940. In 1945 McDonough added 48 cases to this series and pointed out the gradual increase in the use of the drug. He stressed the significance of this procedure as a possible cause of vaginal bleeding in early pregnancy. Johnson reported two cases seen in New Orleans in 1949 and emphasized again the importance of routine speculum examination in every case of vaginal bleeding. Lubin and Waltman added 10 cases in 1951; they also noted the recent gradual increase in incidence and felt that late cases might be confused with placenta previa, such as the one they observed at seven and one-half months' gestation. Duckman and Tortora reported 2 cases from Brooklyn the same year and Bookrajian and Wagner added 4 cases in 1952

from Jersey City. These authors discouraged the use of potassium permanganate vaginally for any reason. The latest report was published by Carney in 1953. He reviewed 20 cases seen in Bellevue Hospital, New York, since 1942. Ten of these required suture ligation of eroded vessels and no abortions were seen. He mentioned one case of cesarean section necessitated by extensive scarring and stenosis of the cervix and upper vagina as a result of the use of potassium permanganate early in pregnancy.

Our series consists of 14 patients seen at University Hospitals of Cleveland in the last 22 months. It is noteworthy that only one of these was seen in 1951, 4 in 1952, and 9 in the first 6 months of 1953. All had amenorrhea, the duration ranging from one day to twenty weeks, and 2 have subsequently delivered at term. Nine in all were pregnant. There was one abortion in a patient whose cervix had been nearly completely eroded away. Four required suture ligation, 2 were treated with vaginal packing only, and 8 required no specific local treatment. Whole blood transfusions were necessary in 4 patients. These experiences are approximately the same as those of other authors in demonstrating the dangers as well as the inefficiency of this agent's use as an abortifacient.

The reasons given for taking the douche or inserting the tablets ranged from treatment of vaginal discharge (5 patients) to admitting attempted abortion (4 patients). In addition there were 4 who stated that they used it to "bring down" their period. Most of them learned the technique through friends, but 2 had been advised by physicians to take potassium permanganate douches for discharge or genitourinary symptoms, and one had been given the tablets by a pharmacist for use as an abortifacient.

Insertion of the whole tablet is apparently the method which is reputed to be most effective in inducing abortion. Dropping the tablet in a douche bag or even crushing the tablet before placing it in the bag does not eliminate the danger of complications. Carney states that it takes up to twenty-five minutes for a tablet to dissolve completely in two quarts of agitated warm water. We had similar results with the whole tablet and also found that even with a crushed 0.3 Gm. tablet, ten minutes was necessary to dissolve all the particles completely. Prior to this elapsed time, any of the tiny particles might enter the vagina through the end of the douche nozzle and cause ulceration.

One of the 14 cases is particularly characteristic:

P. W. (No. 634-197), a 21-year-old Negro woman who had two previous term pregnancies, was admitted to MacDonald House of University Hospitals of Cleveland on April 16, 1953, with a chief complaint of vaginal bleeding. Her last menstrual period was Nov. 28, 1952, and nine hours prior to admission she had inserted a tablet of potassium permanganate into the vagina in an attempt to initiate an abortion. About two hours prior to admission she began to bleed profusely and pass large clots from the vagina. Her blood pressure was 110/50, pulse 94, and respiration 18. Pelvic examination revealed a vagina filled with fresh clots and large ulcers covered by a black, jellylike substance were present on the vaginal mucosa, both anterior and posterior to the cervix as well as on the cervix itself (Fig. 1). There was no bleeding from the undilated cervical os. A small amount of blood was seen oozing from the edge of one of the

blackened ulcers. The uterus was enlarged to the expected size for a twenty weeks' gestation. Her hemoglobin was 8.0 Gm. Oxidized cellulose was placed over the ulcerations and a gauze pack was inserted. The patient received penicillin; the pack was removed in 24 hours and there was no further bleeding. She was discharged on the third hospital day to be followed in the outpatient department. Healing was practically complete by the fourth day (Fig. 2).

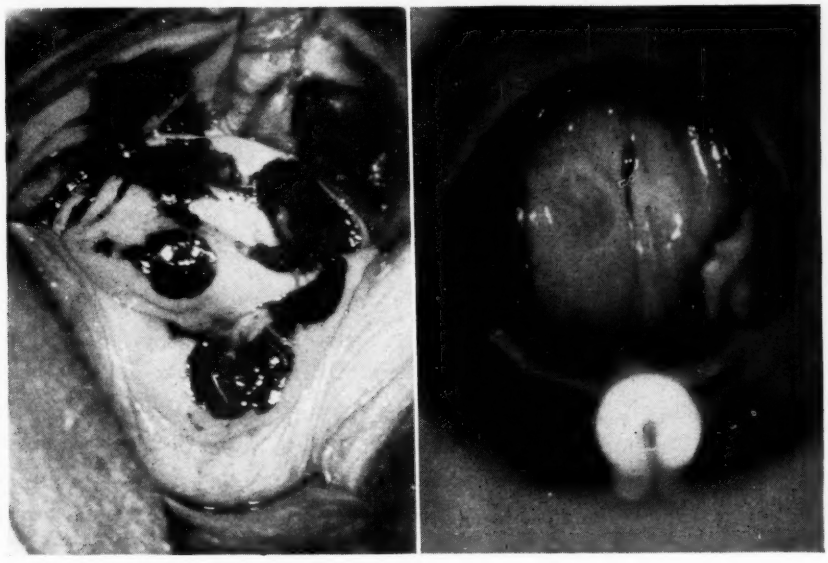

Fig. 1. Fig. 2.

Fig. 1.—P. W. Cervix and vaginal mucosa approximately twelve hours after insertion of a whole potassium permanganate tablet, showing the black covering over punched-out ulcers.
Fig. 2.—The same area four days later. No treatment except oxidized cellulose and vaginal gauze packing.

The diagnosis is usually easy when suspected but can easily be missed without a thorough inspection of the vaginal and cervical mucosa, especially of the vaginal fornices. In this series at least 7 patients gave false histories and were suspected of having threatened or incomplete abortions prior to vaginal speculum examination. It is readily understood why an unsuspecting physician might proceed with a dilatation and curettage, unknowingly interrupting an intact pregnancy. The typical lesion is a sharply punched-out ulcer covered by a black jellylike material when seen early and if 48 hours has elapsed it may appear to be a shallow ulceration. The cervical mucosa may be involved but the os is usually undilated and no blood is coming from a higher area.

Hemorrhage subsequent to erosion into vessels deep in the vaginal mucosa can in itself be a serious matter, requiring emergency measures such as transfusion, general anesthesia, and suture of bleeding points. In our series 6 patients had hemoglobin of less than 10 Gm. when first seen and one had a hemoglobin of 6.5 Gm. after she had received 1,000 c.c. of whole blood. Perhaps of even more serious significance is the fact that two deaths have been reported by Jetter and Hunter: one followed the intravaginal use of a

saturated solution of potassium permanganate as an abortifacient and the second was almost surely of a similar nature. They postulated that in acute potassium permanganate poisoning death may be caused by circulatory collapse incident to severe local injury and by intravascular hemolysis and/or hyperpotassemia due to local absorption or release incident to acute hemolysis.

Green and Warr have reported 24 instances of attempted suicide by ingestion of potassium permanganate crystals or tablets, 23 in women; nearly all had gained possession of the drug for use in preparation of vaginal cleansing douches.

With these reported complications in mind and from our own experiences, we are of the opinion that prescribing, advising, or dispensing the drug for gynecologic treatments should be discontinued. Its value in other fields should be very critically analyzed with the possibility of completely discontinuing its medicinal use.

Summary and Conclusions

1. There has been an apparent increase in the vaginal use of potassium permanganate tablets or solutions as an abortifacient.

2. The pharmacology of this drug is reviewed. Locally its reaction on protoplasm releases manganese dioxide, oxygen, and potassium hydroxide; potassium hydroxide has corrosive powers capable of producing serious hemorrhage and shock. Systemically it may cause convulsions and coma, intravascular hemolysis, and hyperpotassemia.

3. The recent reports of complications from its use, including fatal ones, are noted.

4. Fourteen patients in the past 22 months at MacDonald House of University Hospitals of Cleveland were found to have vaginal evidence of damage from the use of this medication. Four of these patients required sutures to control the bleeding and in two the bleeding was controlled by a vaginal pack. Four patients had sufficient blood loss to necessitate whole blood transfusions.

5. Characteristically the vaginal lesions are punched-out ulcerations, covered by a black, jellylike material (manganese dioxide). Vaginal inspection is essential for diagnosis.

6. In many instances the damage apparently followed its use in solution as a cleansing douche. Undissolved fragments of the tablet can pass through the douche nozzle and be deposited on vaginal mucosa.

7. We are of the opinion that the possible dangers of the intravaginal use of potassium permanganate outweigh any possible gynecologic advantages. Other uses should be critically assessed with the possibility of discontinuing its use as a therapeutic agent in medicine.

References

Beckman, H.: Treatment in General Practice, Philadelphia, 1948, W. B. Saunders Company.
Bookrajian, E. N., and Wagner, V.: AM. J. OBST. & GYNEC. 64: 681, 1952.
Carney, B. H.: AM. J. OBST. & GYNEC. 65: 127, 1953.
Duckman, S., and Tortora, J. M.: New York J. Med. 51: 2260, 1951.

Green, D., and Warr, O.: South. M. J. **34**: 1288, 1941.
Jetter, W. W., and Hunter, F. T.: New England J. Med. **240**: 794, 1949.
Johnson, C. M.: New Orleans M. & S. J. **102**: 68, 1949.
Kautz, H. D.: Personal communication from the Council on Pharmacy and Chemistry of the American Medical Association, May 29, 1953.
Krantz, J. C.: Personal communication (June 3, 1953).
Lubin, S., and Waltman, R.: Am. J. Surg. **82**: 227, 1951.
McDonough, J. F.: New England J. Med. **232**: 189, 1945.
Shull, J. C.: AM. J. OBST. & GYNEC. **41**: 161, 1941.
Sollman, T.: Manual of Pharmacology, Philadelphia, 1948, W. B. Saunders Company.
Trussell, R. E.: Trichomonas Vaginalis and Trichomoniasis, Springfield, Ill., 1947, Charles C Thomas.

2105 ADELBERT ROAD (DR. SCOTT)

UTERUS DUPLEX UNICOLLIS*

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ALTHOUGH there is an abundant literature on the subject of congenital anomalies of the female generative tract, there has been relatively little mention of the interesting type known as uterus duplex unicollis, vagina simplex. The discovery of 2 such cases within seven months prompted discussion with other colleagues and 3 additional cases came to light. It therefore seems reasonable to assume that the occurrence of these 5 in a short period of time almost eliminates the element of chance or coincidence. Accordingly, it is with the purpose of stimulating the interest of other clinicians in this subject that this paper, comprising a review of the literature and case reports, is presented.

A practical knowledge of the embryological development of the generative tract is essential in order to understand properly and to evaluate the symptomatology and complicating factors associated with this condition. There is general agreement that the uterus, tubes, and vagina develop from the Müllerian ducts. The details of the process which usually gives rise to the normal tubes, corpus, cervix, and vagina are too well known to justify repetition. During the embryonic stage, many different types of abnormalities may arise dependent upon either absence of improper fusion of these ducts, faulty canalization, or absorption of septa. Consequently, these anomalies vary from the almost normal uterus arcuatus, to the commonly recognized uterus didelphys, where there is a duplication of vagina, cervix, and uterus. It is surprising to note the confusion that exists in the literature with regard to classification and nomenclature. The anomaly here presented is both unusual and deceptive, in that there is no duplication of vagina or cervix, but 2 separate and distinct uterine bodies. According to Dannreuther,[4] another differential criterion in these cases is the presence of an attachment to the bladder between the two corpora. This can be of importance if hysterectomy is undertaken.

It is difficult to ascertain from the literature any true estimate of the incidence of this condition. Until ten years ago, most cases were discovered either at autopsy, at laparotomy, or during a difficult labor. Recent writers (Eisman,[8] Taylor[14]) maintain that anomalies are not as infrequent as was previously supposed. They believe that lack of fusion of Müllerian ducts may be found once in about 15,000 obstetric operations and once in about 2,000 gynecologic operations. From private records, Moore[12] arrives at the con-

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clusion that 1 in 500 or 600 women present some congenital deviation from the normal uterus. The finding of 5 cases of uterus duplex unicollis within a period of seven months by the author and a small group of associates also suggests a higher incidence than might be suspected. From the records at University Hospital, there was a total of 11,324 gynecological admissions from 1933 to 1951. Of this number, 19 patients were found to present anomalies of the uterus, an incidence of 1 in 596. Of these, there were 6 that fulfilled the criteria for the diagnosis of uterus duplex unicollis.

The symptomatology associated with this anomaly parallels that of the anomalies in general. Very commonly there are no symptoms, but there may be complex difficulties which are confusing until the true condition is recognized. As will be noted in the cases to be reported, a prominent symptom is menstrual dysfunction. Unless one of the uterine bodies is rudimentary, menstruation occurs simultaneously from both, although the flow approximates the normal amount for a single uterus. The case reported by Bainbridge[1] is of interest in that menstruation occurred every two weeks, alternating from both cavities. This is a most difficult phenomenon to explain with our current concepts of menstrual physiology. Menorrhagia may also be seen in double uteri and is explained on the basis of an increased area of endometrium—unless there is associated organic pathology. Dysmenorrhea is a common complaint, as is also dyspareunia.

According to recent writers, fertility and frequency of conception are not adversely affected by a double uterus. It is recognized that there is a much higher incidence of abortion in such cases, as high as 50 per cent. Hormonal influences, deficient uterine musculature, or the mechanical influence of the nongravid horn may all be possible factors in the increased tendency to miscarry. It is interesting to note that a decidual cast is formed in the nongravid portion of the double uterus, and may be expelled during the gestational period. At such a time one might suspect miscarriage, but further observation reveals the continuation of the pregnancy. It is also possible for a pregnancy to occur in each horn, one of which may abort, while the other continues normally to term. Curettage of the living ovum has been reported with this error in diagnosis. The increasing reports of pregnancy in the rudimentary horn of a double uterus warrant special consideration. The deficient musculature of this maldeveloped portion often gives way with the extension of the growing ovum, resulting in a catastrophic rupture similar to that in isthmic ectopic gestation, except that it may occur at a later period in pregnancy. The diagnosis of this complication presents difficulties unless the double corpus is known to exist. Before rupture, such a case is often considered to be a myoma complicating normal pregnancy. When pregnancies in such uteri reach term, there is a definite increase in the complications of labor and delivery. Malpositions of the fetus, particularly breech and transverse, are common. Prolonged labor, rigidity of the cervix, rupture of the uterus due to a deficient musculature, atony in the third stage with postpartum hemorrhage, retained or adherent placenta, and obstruction by the nongravid horn are some of these complications. It must be emphasized that normal labors

and deliveries often occur under such circumstances. The important point is to recognize the causative factor when such complicating features occur in the presence of such an anomaly.

The diagnosis of uterus duplex unicollis is not easy, and very seldom is made on physical findings alone. Often the clinician is misled by the normal appearance of the vagina and cervix. When a septate vagina or cervix is found, he is alerted at once to the possibility of further congenital malformation. This condition is most often mistaken for a myoma of the uterus because of the broadening and apparent irregularity of the corpus.

We are indebted to Jarcho[11] for his pioneer work in the development of uterosalpingography as an important diagnostic aid. Since 1927, he has popularized this technique, and has given considerable impetus to its use in the diagnosis of congenital anomalies. It is the most certain method by which an accurate diagnosis can be made prior to exploration. This point cannot be overemphasized, as will be demonstrated in the appended case reports. In this series, the fractional method of uterosalpingography originated by Hyams, employing either Lipiodine or Lipiodol, was used. No serious, harmful effects attributable to the oily media have been noted in over twenty years at University Hospital.

With respect to therapy, each case must be evaluated as an individual problem. Although there can be no set rules or regulations to govern the management, most authors are in accord with the belief that certain general principles should be followed. In the first place, the discovery of this anomaly does not indicate surgery in the absence of other organic pathology. Second, if indicated, and whenever possible, surgical procedures should be of the conservative type, because these patients are usually in the childbearing group. Even dilatation and curettage may result in perforation of the uterus when one horn is rudimentary. It is generally conceded that metroplasty is a procedure that is not warranted in view of the poor results, especially when performed for infertility. However, the case reported by Eisman[8] is of note in that metroplasty was performed, the abdomen having been entered for other reasons. This patient, who had been infertile, became pregnant after the operation.

An interesting and, as far as can be determined, hitherto unreported observation in the analysis of anomalies of the uterus, is the rather frequent occurrence of uterine myomas. In this series, which includes 23 cases from University Hospital, there were 8 proved myomas, and 5 others suggested by uterographic studies. In percentage (45 per cent) this is a high incidence, and may be of importance in the explanation of associated menorrhagia. The conservative surgical procedure most often performed is hemihysterectomy or myomectomy, and the results have been reported as satisfactory except for the relief of infertility. Should symptoms warrant surgery, and if further pregnancies are not desired, a total hysterectomy should be performed. It is of interest to note that no malignancy of the uterus was encountered among these cases.

The following case reports are presented as illustrative:

CASE 1.—H. L., aged 36 years, had been married two years with no pregnancies. Her chief complaint was sterility. Menstruation began at the age of 12 years and occurred thereafter at thirty-day intervals. The flow lasted four days and was associated with occasional mild dysmenorrhea. Pelvic examination was negative except for physiological anteflexion of what was thought to be a normal-sized uterus. A complete sterility work-up was performed with the following positive findings: subnormal sperm; questionable cervical hostility as determined by Huhner tests. After an amenorrhea of six weeks, she had a spontaneous miscarriage, followed by a dilatation and curettage in 1947, with the pathologic report showing products of conception. The operator described the uterus as retrocessed and retrodisplaced. The sterility work-up was repeated in 1951, with essentially the same findings. Uterosalpinogram revealed a double uterus with nodular filling defects in the right horn (Fig. 1).

Diagnosis: Uterus duplex unicollis, with myomas (x-ray diagnosis).

Fig. 1.—Uterus duplex unicollis with evidence of myomatous involvement in the right horn.

CASE 2.—B. V., aged 41 years, gravida i, para i, had had a full-term breech delivery. The placenta did not separate, necessitating manual removal. The chief complaint was left lower quadrant pain, severe for the last two days. Menstruation started at 13 years and occurred every thirty days. The flow was moderate in amount with no pain and lasted from three to five days. Pelvic findings on Dec. 6, 1951, showed a normal vagina and cervix. The uterus was not outlined per se, but seemed to be fused with bilateral, firm adnexal masses, suggestive of ovarian tumors. On Dec. 7, 1951, a laparotomy was performed, and a uterus duplex unicollis was found with multiple uterine fibroids, the largest being the size of an apple in the right horn. Hemihysterectomy was performed.

Diagnosis: Uterus duplex unicollis with multiple fibromyomas (surgical and pathological diagnosis).

CASE 3.—A. M. was 31 years of age, gravida 0. Menses started at the age of 12 years, occurred every twenty-eight days, and lasted six days with normal flow. She was seen after an amenorrhea of six weeks because of vaginal bleeding of seven days' duration associated with left lower quadrant pain. Pelvic examination on April 31, 1951, revealed moderate vaginal bleeding. The cervix was clean and not tender on motion. The uterus was anterior, soft, and slightly larger than normal. The right adnexa were negative, but there was definite tenderness associated with a boggy mass in the left fornix. The impression was that of a left ectopic gestation. Laparotomy on April 31, 1951, disclosed normal adnexa with a corpus luteum in the left ovary. The uterus was composed

of two separate bodies. The left corpus was definitely larger and much softer than the right. Dilatation and curettage were performed, and products of conception were recovered. A uterosalpingogram was performed on Oct. 4, 1951 (Fig. 2).

CASE 4.—A. H., aged 35 years, gravida v, para 0. The chief complaint was habitual abortion. She had had five spontaneous abortions between ten and sixteen weeks in the past five years. On every occasion a curettage had been carried out. Menstruation began at 13 years and occurred at twenty-eight-day intervals. The flow was normal and lasted five days with occasional mild dysmenorrhea. Pelvic examination revealed a normal perineum and vagina. The cervix was clean; the uterus was felt to be retrocessed but

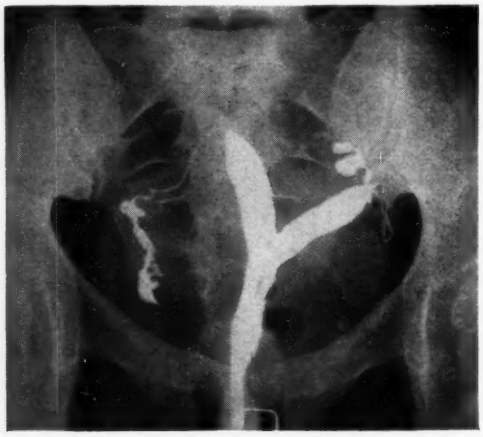

Fig. 2.—Uterus duplex unicollis also proved by laparotomy.

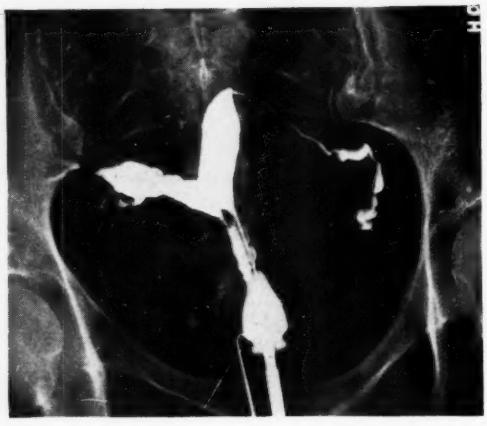

Fig. 3.—Uterus duplex unicollis with evidence of myomatous involvement in the right horn.

anterior and broader than normal. The adnexa were grossly negative. A complete work-up was done, including urinalysis, blood count, basal metabolic rate, endometrial biopsy; all proved negative. Therapy to prevent abortions included bed rest and administration of stilbestrol, corpus luteum extracts, vitamins, and thyroid. Following the last miscarriage in 1950, a suggestion of irregularity on examination of the uterus prompted uterosalpingogram with resultant findings as noted in Fig. 3.

Diagnosis: Uterus duplex unicollis, possible myoma of right uterus (x-ray diagnosis).

CASE 5.—S. C., aged 37 years, had one child fourteen years ago. Her complaints included lower abdominal pain, irregular menses, primary dysmenorrhea with increasing severity, and severe dyspareunia. Menses began at 12 years, lasted four days, occurring every twenty-one to twenty-eight days. Prior surgery included an appendectomy and resection of an ovarian cyst four years ago, and a repair of an inguinal hernia two years ago.

Pelvic examination disclosed a well-repaired perineum and a cervix everted and clean. The uterus was anterior, large and normal in size, with irregularity in contour and tender on motion. The adnexa were within normal range. Tenderness was noted in the left uterosacral region. The clinical impression was adenomyosis. Uterosalpingogram performed Feb. 26, 1953, revealed uterus duplex unicollis with a suggestion of polyps in the right corpus (Fig. 4).

Because of her severe dysmenorrhea and dyspareunia, laparotomy was decided upon, and total hysterectomy was performed on April 8, 1953. The pathological report was uterus duplex unicollis with fibromyoma.

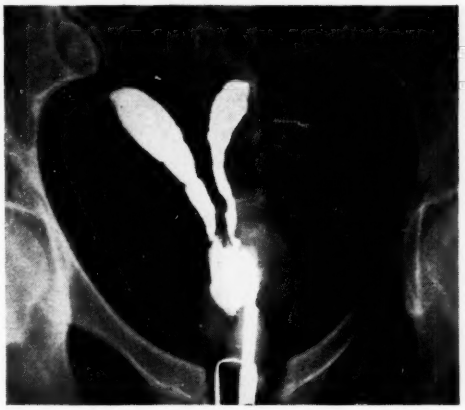

Fig. 4.—Uterus duplex unicollis.

In summarizing the clinical aspects of these cases, the following observations are reaffirmed. The diagnosis was not suspected clinically in any case. It was made by accident in all cases, by x-ray in 3, as part of a complete infertility work-up in 2, while it was not made until laparotomy in the other 2. The fact that frequency of conception is usually not adversely affected is well exemplified by noting that each patient had at least 1 pregnancy. There was a total of 9 proved pregnancies which terminated as follows: 2 full-term vaginal deliveries, one a breech presentation with complications in the third stage, and 7 spontaneous miscarriages, an incidence of 77 per cent. There was a total of 7 curettages all of which were for incomplete abortions. It is interesting that 6 of these were performed prior to discovery of the double uterus. Two cases were proved to have myomas by laparotomy, while two had hysterographic evidence of a fibromyoma. From the standpoint of therapy, it is to be noted that 3 out of the 5 presented no indication for surgery. In Case 2 this condition was not recognized preoperatively and the associated fibroids were treated conservatively. In Case 5, the severe and incapacitating

progressive type of dysmenorrhea and dyspareunia constituted the basis for surgical intervention. The patient's age, symptoms, lack of desire for further pregnancies, and the associated myoma indicated hysterectomy.

Summary and Conclusions

1. The criteria for the diagnosis of uterus duplex unicollis, vagina simplex are reviewed and presented.

2. The discovery of 5 cases within a seven-month period suggests a higher incidence of this anomaly than has heretofore been noted in the literature.

3. The high incidence of abortion is confirmed.

4. The use of uterosalpingography as an aid in diagnosis is invaluable.

5. The associated high incidence of myomas is discussed.

6. Conservative therapeutic management should be the rule, not the exception, in the treatment of these anomalies.

I would like to thank Dr. L. L. Mackenzie, Dr. J. N. Tesi, and Dr. Peter La Mariana, for permitting me to include Cases 2, 3, and 4.

References

1. Bainbridge, W. S.: Am. J. Obst. & Gynec. **7**: 285, 1924.
2. Crossen, H. S., and Crossen, R. J.: Diseases of Women, ed. 9, St. Louis, 1941, The C. V. Mosby Company, p. 748-750.
3. Curtis, A. H.: A Textbook of Gynecology, ed. 4, Philadelphia, 1942, W. B. Saunders Company, pp. 628, 632.
4. Dannreuther, W. T.: Am. J. Obst. & Gynec. **14**: 376, 1927.
5. Davis, J. L., and Cellan-Jones, C. J.: Brit. M. J. **2**: 59, 1927.
6. De Lee, J. B., and Greenhill, J. P.: The Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Company, pp. 532-533.
7. Dodds, G. S.: The Essentials of Human Embryology, New York, 1929, John Wiley & Sons, pp. 211-234.
8. Eisman, J. R.: Am. J. Obst. & Gynec. **47**: 559, 1944.
9. Greenhill, J. P.: Office Gynecology, ed. 3, Chicago, 1943, The Year Book Publishers, Inc., pp. 123-133, 144.
10. Jarcho, J.: Surg., Gynec. & Obst. **45**: 129, 1927.
11. Jarcho, J.: M. J. & Rec. **137**: 235, 1933.
12. Moore, O.: South. M. J. **34**: 610, 1941.
13. Puddicombe, J. F.: Surg., Gynec. & Obst. **49**: 799, 1929.
14. Taylor, H. C.: Am. J. Obst. & Gynec. **46**: 388, 1943.
15. Titus, P.: The Management of Obstetric Difficulties, ed. 2, St. Louis, 1940, The C. V. Mosby Company, pp. 449-450.
16. Hyams, Mortimer N.: Personal communication.

THE ELECTRICAL ACTIVITY OF THE HUMAN UTERUS IN NORMAL AND ABNORMAL LABOR

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PART I. THE TYPE OF ELECTRICAL ACTIVITY ASSOCIATED WITH VARIOUS TYPES OF CASES

IN 1950 there was described a device[1] (the Electrohysterograph or EHG) for recording the electrical activity of the human uterus, together with the findings in 78 patients. At that time it was demonstrated that labor which was normal by clinical standards was associated with a certain type of electrical activity, and that this activity appeared to be absent in 8 cases of clinical uterine inertia. Since that time, the Electrohysterograph has been used to study 556 additional patients, both normal and abnormal, and the results of this study are presented in this paper.

There have been two other studies of the electrical activity of the human uterus reported since 1950. Halliday and Heyns[2] recorded the electrical potential on the surface of the abdomen using an amplifying and recording system which would register both slow and rapid changes in potential. They demonstrated changes in the electrical potential associated with uterine contractions of a type similar to those demonstrated by Steer and Hertsch previously with the direct current amplifier. These waves demonstrate a slow shift of potential of rather irregular character. Superimposed upon these slow shifts of potential are the small waves which are studied by the apparatus used in the present series of cases. Levy-Solal, Morin, and Zacouto[3] recorded the electrical activity on the abdominal wall during labor using an apparatus similar to the one in use in the present study. Their technique differed in that the electrodes were placed on each cornu of the fundus. They were able to record three different types of electrical activity which they were able to correlate with normal labor and with uterine inertia.

It can be seen that there is electrical activity associated with uterine contraction during labor which can be recorded by electrodes placed on the abdominal wall. This is of two types as demonstrated previously,[1] but the more rapid activity at a frequency of about ⅓ cycle per second produces a consistent pattern from contraction to contraction, whereas the slow activity in which there may be but one or two waves associated with a given contraction does not present itself in a reproducible pattern. It has seemed more worth while to the author, therefore, to concentrate upon the electrical activity at ⅓ cycle per second.

Material

The problem of labor has two aspects, each of which may be considered separately but each of which is related directly to the other in determining the final outcome of labor. One aspect, which might be called "dynamic," has to do with the forces of labor, particularly the efficiency of uterine contraction. The other aspect, which might be called "static," has to do with the mechanical problem of the relation of the size and position of the child to the amount of room available in the pelvis. It is obvious that delivery from below cannot be accomplished in extreme degrees of disproportion despite the most efficient uterine contractions, and similarly delivery from below cannot be accomplished in extreme degrees of uterine inertia even when disproportion is absent. There are all possible gradations between these two extremes. In studying the electrical activity of the uterus it is therefore necessary to evaluate the clinical course of labor, and in addition to measure the degree of disproportion present.

TABLE I. TYPES OF CASES STUDIED

TYPE OF CASE	EHG DURING LABOR ONLY	EHG BEFORE LABOR ONLY	EHG BEFORE AND DURING LABOR	TOTAL
1. Normal labor	307	58	3	368
2. Disproportion, without inertia or Pitocin	42	6	4	52
3. Uterine inertia, without disproportion or Pitocin	6	0	0	6
4. Uterine inertia, with disproportion, without Pitocin	5	0	0	5
5. Uterine inertia, without disproportion, with Pitocin	24	2	0	26
6. Disproportion, without inertia, with Pitocin	8	0	0	8
7. Uterine inertia, with disproportion, with Pitocin	14	0	0	14
8. Pitocin infusion for induction of labor, successful	42	0	0	42
9. Pitocin infusion for "slow labor"	14	0	0	14
10. Pitocin infusion for induction of labor, failed	12	0	0	12
11. Late pregnancy, no contractions	0	6	0	6
12. Premature separation of placenta	3	0	0	3
Total	477	72	7	556

The cases studied by this method were all taken from the Labor Rooms of the Sloane Hospital for Women. There were 536 ward cases and 20 private cases, for a total of 556 patients. These patients were studied as they became available at varying stages of pregnancy and labor, and the series therefore represents a random sampling. The series was divided into ten groups, as shown in Table I. This classification is based upon the clinical impression of labor, upon the results of x-ray pelvimetry (performed when disproportion was suspected), and upon the use (or lack of use) of a Pitocin infusion. The Electrohysterograph records were *not* used to classify the labor as *normal* or *abnormal.*

Apparatus

1. The Electrohysterograph.[1]—This is an instrument which records changes in electrical potential on the surface of the abdomen during labor.

Electrodes made of solder pellets 2 mm. in diameter are placed on the abdominal wall in pairs about 6 cm. apart, in such a way that one pair lies over the left uterine cornu, another pair over the right uterine cornu, and the third pair over the midline of the uterine fundus. A ground electrode is placed on the flank of the patient. These electrodes are applied over electrode jelly and are held in place by adhesive tape. The electrodes feed into three vacuum tube differential amplifiers which in turn drive a three-channel recorder.

2. X-ray Pelvimetry.—This consists of two anteroposterior stereoscopic views of the pelvis by the Caldwell-Moloy technique, a standing anteroposterior view, and a standing lateral view with a marker in the gluteal fold. The relation of the head to the pelvis is studied, and when disproportion is present the degree of disproportion is estimated by the circle method described by Moloy and Steer.[4] In this method the index of disproportion at the inlet is the numerical difference in centimeters between the diameter of the circle which fits the inlet and the diameter of the fetal head. Disproportion in the midpelvis is estimated by calculating the difference between the interspinous diameter and the diameter of the head, and then correlating this difference with the shape and position of the sacrum and the subpubic arch.

Method

An Electrohysterograph recording was obtained on each patient. In cases of special clinical interest, the recording was repeated, so that 655 recordings were made on the 556 patients. Each case was managed on the basis of the clinical findings, and when disproportion was suspected x-ray pelvimetry was performed. The Electrohysterograph findings were *not* allowed to influence the method of management, but the x-ray findings were used in the choice of method of delivery.

The Electrohysterograph recording (EHG) was analyzed by noting the location, duration, frequency, and amplitude of the electrical waves. These waves are seen only during a contraction, and are seen whether the contraction is one of true labor at term, premature labor, or false labor. Between contractions there is seen a relatively smooth tracing, in which the electrocardiogram can usually be seen and in which smooth, slow waves associated with respiration may also be seen. The waves may be present at one or all of the three pairs of leads. The frequency of the waves varies from ⅕ to 2 cycles per second. The amplitude of the waves varies from 50 to more than 500 microvolts. The total duration of the characteristic electrical activity varies directly with the clinical duration of the contraction. (It was noted previously that the electrical activity begins simultaneously with mechanical contraction, that pain begins ten to twenty seconds later, that the electrical activity and the pain end simultaneously, at which time relaxation starts, and that relaxation is not completed for another fifteen to thirty seconds.)

The method of analysis may be illustrated in Fig. 1. In this case, the upper tracing *R* is taken from the pair of electrodes placed over the right cornu, the middle tracing *C* is taken from the pair of electrodes placed in the midline of the fundus, and the lower tracing *L* is taken from the pair of electrodes placed over the left cornu. The characteristic waves are seen beginning just before point *A*. The waves are present in all three leads. The frequency varies irregularly (it is not the regular frequency of the electrocardiogram seen so clearly in the intervals between contractions). The pattern is slightly different in all 3 leads, but the shape of the waves is characteristic of the uterine waves. It is necessary, therefore, to take an over-all estimation of the frequency. The duration of electrical activity at *R* is 25 seconds, during which time there are 12 uterine waves, for a frequency

of 0.48 cycle per second. At *C* there are 12 waves in 29 seconds, a frequency of 0.41 cycle per second. At *L* there are 14 waves in 29 seconds, a frequency of 0.48 cycle per second. The over-all frequency in this case may be said to be between 1/2 and 1/2.5 cycle per second. Since this varies from lead to lead in the same patient, and from patient to patient, over a range between 1/2 and 2 cycles per second, it is not worth while to calculate the frequency to several decimal places. The fraction expresses the frequency well enough from a practical point of view. The same consideration holds in determining the amplitude of the waves. In Fig. 1 the waves vary from about 50 to about 350 microvolts.

The "strength" of the electrical activity may also be described qualitatively as "strong," moderate," "weak," or "absent." This division is quite arbitrary, and is based on the amplitude of the waves as follows: strong—amplitude mainly above 500 microvolts; moderate—amplitude mainly between 200 and 500 microvolts; weak—amplitude mainly below 200 microvolts; and absent—no recognizable uterine waves. In this case, then, the *location* of the activity is at all three leads, the *duration* is 25 to 30 seconds, the *frequency* is about 1/2 cycle per second, and the *amplitude* is 50 to 350 microvolts. The strength is moderate.

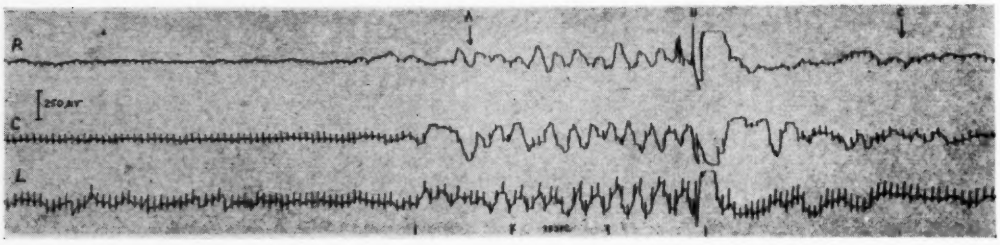

Fig. 1.—Electrohysterograph in a case of normal labor. Upper tracing *R* from right cornu (see text), middle tracing *C* from midline of fundus, lower tracing *L* from left cornu. Reference electrode on left flank. Calibration 250 microvolts. Time intervals 10 seconds. At point *A*, pain began and uterus was felt to harden. At point *B*, pain stopped and relaxation began. Relaxation was completed at point *C*. Note that electrical activity began before pain was felt, and that electrical activity and pain stopped simultaneously.

Following analysis of the EHG according to this method, the cases were then divided into groups (as shown in Table I) according to the clinical estimation of labor and according to the degree of disproportion present. The clinical estimation of labor was made by those members of the obstetrical staff engaged in the care of the patient. The investigator took no part in this estimation at the time the patient was seen, and did not alter this estimation on the basis of the EHG findings. The x-rays were read and the degree of disproportion estimated by those members of the staff who usually do so, and the investigator did take some part in this as part of his usual functions. It was then possible to describe the results in two ways: (1) according to the type of electrical activity found in various kinds of labor, and (2) according to the outcome of labor when classified according to type of electrical activity and degree of disproportion.

Results According to Type of Electrical Activity

Electrical activity was found to be *present* in 544 cases and *absent* in 12 cases. The type of electrical activity associated with the various types of cases is shown in Table II. It may be noted that electrical activity was *absent* only in certain cases of uterine inertia (a total of 6 cases) or when there were no uterine contractions at all present (6 cases).

TABLE II. STRENGTH OF ELECTRICAL ACTIVITY IN VARIOUS TYPES OF CASES

	STRONG	MODERATE	WEAK	ABSENT	TOTAL
1. Normal labor:					
During labor	38	218	51	0	307
Before labor	0	32	26		58
Before and during labor	See text				3
2. Disproportion, without inertia or Pitocin:					
During labor	5	23	14	0	42
Before labor	0	3	3	0	6
Before and during labor	See text				4
3. Uterine inertia, without disproportion or Pitocin	0	2	2	2	6
4. Uterine inertia, with disproportion, without Pitocin	0	2	2	1	5
5. Uterine inertia, without disproportion, with Pitocin	0	15	10	1	26
6. Disproportion, without inertia, with Pitocin	0	6	2	0	8
7. Uterine inertia, with disproportion, and Pitocin	0	6	7	1	14
8. Pitocin infusion for induction of labor, successful	0	34	8	0	42
9. Pitocin infusion for "slow labor"	0	10	4	0	14
10. Pitocin infusion for induction of labor, failed	0	5	6	1	12
11. Late pregnancy, no contractions	0	0	0	6	6
12. Premature separation of placenta	See text				3
Total	43	356	135	12	556

1. Normal labor, 368 cases (307 with records during the final labor, 3 with records both before and during the final labor, and 58 with records during false labor): These were patients with clinically normal labor, and with no evidence of disproportion, all of whom were delivered spontaneously or by low forceps. All of these cases showed irregular waves in the Electrohysterograph record, at a *frequency* of ⅕ to 2 cycles per second, the usual frequency being ⅓ cycle per second (Fig. 1). The *amplitude* varied from 50 to 500 microvolts, varying directly with the clinical strength of the uterine contraction. The *duration* of electrical activity varied with the clinical duration of the contraction. The *location* of the electrical activity (at one or more of the three pairs of electrodes) varied to some extent with the time at which the record was taken. In early labor electrical activity is usually found at one or two leads, and in clinically strong, active labor at all 3 leads, but this is not invariable. Some patients start labor with activity present at all three leads.

The records were divided as previously described according to the "strength" of the electrical activity. In the 307 cases recorded during labor, activity was strong in 38, moderate in 218, and weak in 51 cases. There is a general but not a specific correlation between the strength of the uterine activity and the duration of labor. The statistical median of length of labor with strong activity is eight hours, with moderate activity twelve hours, and with weak activity fourteen hours. The distribution of length of labor according to strength of electrical activity is shown in Fig. 2. It is seen that the labor tends to be shorter as the activity is stronger, but there are such wide variations from these figures that no specific prognosis for length of labor in an individual case can be made from the strength of the electrical record. The cases were then divided into groups according to the time in labor when the record was obtained. The results are shown in Fig. 3. The strength of the electrical activity is predominantly moderate in all groups, but it is obvious that uterine contractions either during or before the final labor may be ac-

companied by any strength of electrical activity. In the normal case, the amplitude usually increases as labor progresses, so that weak activity may be found in early labor, and strong activity near the end of labor, but these findings are not invariable, some patients with weak activity nevertheless making rapid progress. It appears, then, that the *frequency* of the electrical activity, at ½ to 2 cycles per second, is indicative of normal uterine activity, and the amplitude of the waves is of secondary importance.

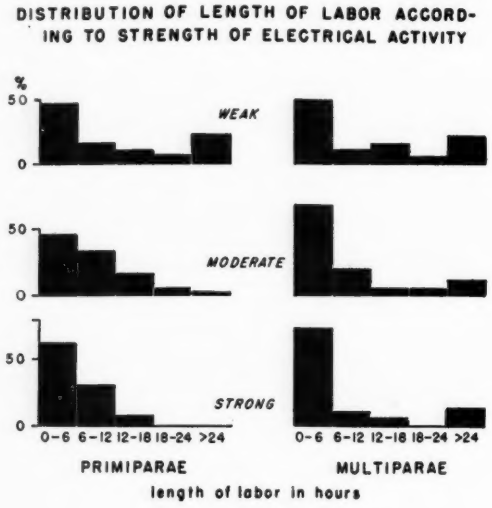

Fig. 2.

There were 3 cases in which records were obtained both before and during the final labor. One multipara had weak activity with fifteen-minute contractions three weeks before the final labor, and then had moderate activity three and one-half hours before a normal delivery (labor five and one-quarter hours). The second patient, a primipara, had moderate activity one day before the final labor, and again had moderate activity one and one-half hours before a normal delivery (labor nine and one-half hours). The third patient, a multipara, had weak activity 3 weeks before the final labor, and again had weak activity four and one-half hours before a normal delivery (labor thirteen and one-half hours).

TABLE III. STRENGTH OF ELECTRICAL ACTIVITY IN CASES STUDIED DURING FALSE LABOR

STRENGTH OF ELECTRICAL ACTIVITY	TIME, BEFORE FINAL LABOR, AT WHICH EHG RECORD WAS OBTAINED				TOTAL
	ONE DAY OR LESS	2 TO 7 DAYS	8 TO 30 DAYS	MORE THAN 30 DAYS	
Strong	0	0	0	0	0
Moderate	19	5	6	2	32
Weak	14	4	7	1	26
Total	33	9	13	3	58

There were 58 patients who were subsequently delivered easily from below after a normal labor, in whom EHG records were obtained only during false labor. All were having uterine contractions of varying degrees of frequency and duration at the time the record was obtained. The electrical activity varied markedly. There was activity in only one lead in 6 cases, in 2 leads in 14 cases, and in all 3 leads in 38 cases. The activity was strong in no case, moderate in 32 cases, and weak in 26 cases. These cases were divided accord-

ing to time before labor at which the record was taken, as shown in Table III. It is seen that no patient had a record of strong activity and that there are approximately equal numbers of those with records of moderate and weak activity in each group. It seems that the time before true labor at which contractions occur does not determine the strength of the electrical activity which accompanies these contractions.

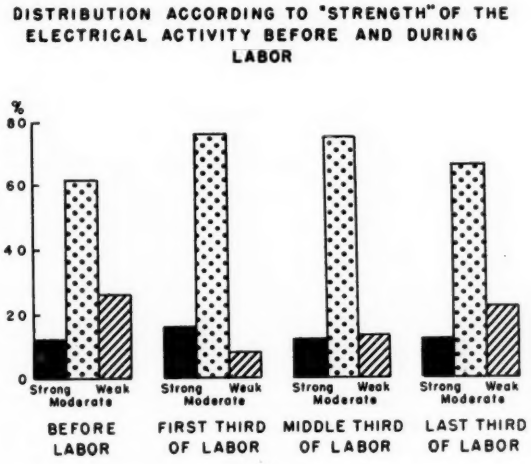

Fig. 3.

2. Disproportion without uterine inertia and without Pitocin, 52 cases: These are cases in which the labor was clinically normal, but in which disproportion was demonstrated to be present by x-ray pelvimetry. All of these cases showed the characteristic uterine waves at about ⅓ cycle per second. The outcome of labor and method of delivery are not related to the quality of the electrical activity. There is a direct correlation between the degree of disproportion and the method of delivery.

There are 42 cases in which the EHG was obtained during labor. The labor was qualitatively strong in 5 cases, moderate in 23 cases, and weak in 14 cases.

Ten patients were delivered spontaneously or with low forceps. The index of disproportion at the inlet varied from 1.2 to 1.6 cm. in 8 cases, and 2 had moderate narrowing of the midpelvis. The average length of labor was sixteen and one-half hours, the median fourteen hours. Four of these patients had strong activity, and 6 had moderate activity.

Four patients were delivered by midforceps, one with a difference at the inlet of 0.6 cm. and a narrowed midpelvis, labor of twenty-one hours, electrical activity moderate; another with a difference of 1.4 cm. and a narrowed midpelvis, labor of twelve hours, and activity moderate; and 2 with markedly narrowed midpelves, after labors of twenty-three and eighteen hours, the first with strong and the second with moderate activity.

Twenty-eight patients were delivered by cesarean section. Twelve of these had inlet disproportion with a difference at the inlet of 1.0 cm. or less. The average length of labor was fourteen and one-half hours, the median fourteen hours. Electrical activity was strong in none, moderate in 6, and weak in 6. Twelve had severe midpelvic contracture, with an average duration of labor of eighteen hours, and a median of sixteen hours. The electrical activity was strong in none, moderate in 7, and weak in 5. One patient with a difference at the inlet of 1.2 cm. and a narrowed midpelvis had a labor of fourteen hours, with weak activity. One patient with breech presentation, 1 with face presentation, and 1 with brow presentation, associated with abnormal pelves, had labors of four, seven, and eleven hours. The activity was weak in each.

There were 4 cases in which records were obtained both before and during labor. In the first of these, there was strong activity twenty-five hours before delivery, and weak activity two hours before delivery. Labor lasted eighteen hours, and delivery was by cesarean section, with an index of disproportion at the inlet of 1.0 cm. In the second case, there was weak activity five weeks before delivery, and moderate activity seven hours before delivery. Labor lasted forty hours. Delivery was by cesarean section after failed forceps, with the index of disproportion at the inlet 0.3 cm. In the third case, there was weak activity twenty-eight hours before delivery, and weak activity again four hours before delivery. Labor lasted twenty-seven hours. There was a breech presentation, with lack of descent, and delivery was by cesarean section. In the fourth case, there was weak activity sixteen days before delivery, and moderate activity four hours before delivery. Labor lasted fifteen and one-half hours. There was a spontaneous delivery, with an index of disproportion at the inlet of 1.2 cm.

There were 6 cases in which records were obtained only before labor began. In one case two records were taken. Three cases showed moderate activity, and 2 showed weak activity. One case showed weak activity forty days before delivery, and moderate activity thirty-one hours before delivery. Five of these patients were finally delivered by cesarean section. The index of disproportion at the inlet was 1.0 cm. in 2 cases, and 1.3 cm. in 1 case. One patient had an index of disproportion at the inlet of 1.6 cm. with a narrow midpelvis, and one had an adequate inlet but a narrow midpelvis. One patient was delivered spontaneously, with an index of disproportion of 1.6 cm. at the inlet.

In these cases, clinically normal labor was associated with normal uterine electrical activity, and the outcome of labor was determined by the degree of disproportion. It is interesting that 4 of the 10 patients who were delivered rather easily from below had strong activity, but these also had the smallest degrees of disproportion.

3. Uterine inertia without disproportion, and without Pitocin, 6 cases: These were cases diagnosed clinically as uterine inertia, in which no treatment was given for the uterine inertia (neither stimulation nor sedation). In none of these cases was there evidence of disproportion. Four of the cases showed electrical uterine activity (moderate in 2 and weak in 2), and 2 patients showed *no* electrical activity.

Three of these (2 with moderate and 1 with weak activity) were delivered spontaneously or by low forceps—one multipara after a labor of fifteen hours and 2 primiparas after labors of thirty and thirty-seven hours. One primipara (with weak activity) was delivered by midforceps after twenty-four hours. Two patients showed *no* electrical activity during labor, although regular, painful contractions occurred. Cesarean section was performed in both cases, after a labor of sixteen hours in one instance and twenty-two hours in the other.

4. Uterine inertia with disproportion, and without Pitocin, 5 cases: These were cases with x-ray evidence of disproportion, and clinical uterine inertia. Four of these cases demonstrated electrical activity, which was moderate in 2 cases and weak in 2, and one case demonstrated *no* electrical activity.

One of these patients, with midpelvic contracture and moderate activity, was delivered by midforceps after twenty-nine hours of labor. Three were delivered by cesarean section. One of these had midpelvic contracture and a labor of thirty-six hours, during which the electrical activity was moderate. The second had a difference at the inlet of 1.3 cm. and a labor of twenty-one hours, during which the activity was weak. The third, a multipara, had an oblique lie. She was in and out of desultory labor, during which the activity was weak, for eighty-six hours before cesarean section was performed. One case showed *no* electrical activity during labor. This patient had marked midpelvic contracture, and cesarean section was performed after twenty-five hours of labor.

5. Uterine inertia, without disproportion, with Pitocin infusion, 26 cases: These were cases without disproportion, but with clinical uterine inertia, which were treated by Pitocin infusion. Electrical activity was present in 23 of these cases studied during labor, and in 2 cases studied before labor. Among those studied during labor, the activity was strong in none, moderate in 15, and weak in 8. The 2 cases studied before labor showed weak activity. There was no difference in length of labor, or in duration of the Pitocin infusion, between those with moderate and those with weak electrical activity.

Spontaneous or low forceps delivery occurred in 18, the labors varying from twenty-five to sixty hours (except in one case of ten hours where marked inertia was produced by spinal anesthesia and Pitocin was given to counteract the anesthesia). The electrical activity was moderate in 10 and weak in 8. The average length of labor was thirty-five hours, the median thirty-five hours. Pitocin was given for periods of forty minutes to eighteen and one-half hours, the average being three hours, the median three hours.

In 3 cases delivery was by midforceps, after labors of twenty-four, twenty-six and thirty hours. Electrical activity was moderate in all 3. Pitocin was given for forty-five minutes in one case (where the inertia was produced by caudal anesthesia), and for seven hours in both of the other cases. One case of breech presentation was delivered from below after twenty-five hours of labor including four hours of Pitocin. Electrical activity was moderate.

Three patients were delivered by cesarean section. One of these, with a breech presentation, was given Pitocin for two hours and operated upon after fifteen hours of labor. This patient had moderate electrical activity. The second had twins, and was given Pitocin for eighteen hours without satisfactory dilation of the cervix. This patient had moderate activity. The total labor was thirty-two hours. The third had inertia due to caudal anesthesia, which was given for sixteen hours. The Pitocin was given for fourteen hours; total labor lasted thirty-four hours. This patient had weak activity. One patient showed no electrical activity during labor, even during stimulation with Pitocin. Cesarean section was performed after twenty-three hours of labor, which included four hours of Pitocin infusion.

TABLE IV. OUTCOME OF LABOR IN CASES OF DISPROPORTION, WITHOUT UTERINE INERTIA, TREATED BY PITOCIN INFUSION

INDEX OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN INFUSION	ELECTRICAL ACTIVITY
Low Forceps or Spontaneous Delivery.—			
1.4 cm. at inlet	19	1⅞	Moderate
1.5 cm. at inlet	21	4½	Moderate
Midforceps Delivery.—			
1.1 cm. at inlet	11	3¾	Weak
Cesarean Section.—			
1.3 cm. at inlet	36	5	Moderate
1.0 cm. at inlet	23	2¼	Moderate
1.6 cm. at inlet and contracted midpelvis	6	6	Moderate
Contracted midpelvis	48	12	Weak
Breech Extraction.—			
1.4 cm. at inlet	19 (neonatal death)	3	Moderate

6. Disproportion without inertia, with Pitocin infusion, 8 cases: These are cases with disproportion demonstrated by x-ray in which labor was stimulated by Pitocin infusion. Electrical activity was present in all 8 cases, being moderate in 6 and weak in 2. The method of delivery, degree of disproportion,

length of labor, duration of the Pitocin infusion, and strength of electrical activity are shown in Table IV. It is seen that the method of delivery is determined chiefly by the degree of disproportion. Clinically it seemed that strengthening of the labor by the Pitocin infusion aided in overcoming the disproportion in those cases with delivery from below. This was responsible for the neonatal death in the breech presentation.

7. Uterine inertia with disproportion and with Pitocin infusion, 14 cases: These are cases with disproportion demonstrated by x-ray, and with clinical uterine inertia, treated by Pitocin infusion. Electrical activity was present in 13 cases, being moderate in 6 cases, weak in 7, and absent in one. The method of delivery in these cases is shown in Table V. It is seen that the degree of disproportion is directly correlated with the method of delivery, but in addition it is obvious that Pitocin stimulation has allowed rather high degrees of disproportion to be overcome in some cases. In one case with a difference at the inlet of 1.0 cm. ("absolute disproportion") delivery was finally effected by low forceps after five hours of Pitocin, with neonatal death occurring a few hours after delivery because of a lacerated tentorium.

TABLE V. OUTCOME OF LABOR IN CASES OF UTERINE INERTIA AND DISPROPORTION, TREATED BY PITOCIN INFUSION

INDEX OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN INFUSION	ELECTRICAL ACTIVITY
Low Forceps or Spontaneous Delivery.—			
1.6 cm.	28	9	Moderate
1.2 cm.	37	2	Moderate
1.0 cm.	48	5 (neonatal death)	Moderate
1.5 cm.	22	6	Weak
Contracted midpelvis	15	2	Weak
Midforceps Delivery.—			
1.6 cm.	61	13	Moderate
1.7 cm.	36	1	Weak
Contracted midpelvis	18	6	Weak
Cesarean Section.—			
1.1 cm.	24	2	Moderate
Contracted midpelvis	64	10½	Moderate
Contracted midpelvis	120	3	Weak
Contracted midpelvis	37	5	Weak
1.3 cm.	36	8	Weak
Contracted midpelvis	23	4	Absent

8. Pitocin infusion for induction of labor, 42 cases: These were all cases without disproportion in which induction of labor was carried out for the following indications:

Elective—30 cases (4 primiparas)

Toxemia—8 cases (4 primiparas)

Premature rupture of membranes—2 cases, both primiparas

Diabetes—1 primipara

Hiatus hernia—1 multipara.

Electrical activity was present in all cases, being moderate in 34 cases and weak in 8. Delivery occurred spontaneously or by low forceps in all cases.

9. Pitocin infusion to stimulate "slow normal" labor, 14 cases: These were all cases without disproportion but with slow labor, in which speeding up of the labor was indicated clinically, usually because a labor lasting over twenty-

four hours was anticipated. These would have become cases of uterine inertia if they had not been treated early. All showed electrical activity, which was moderate in 10 cases and weak in 4. All were delivered easily from below. The length of labor varied from six to twenty-four hours, and the Pitocin was given for periods of forty minutes to eight hours.

10. Failed Pitocin infusion, 12 cases: These were 5 multiparas and 7 primiparas in whom Pitocin induction was attempted without success. Electrical activity was moderate in 5 cases, and weak in 6 cases, although the inductions failed. One patient showed no electrical activity. All of these patients were subsequently delivered from below, labor being successfully induced in 4 cases, and beginning spontaneously in 8.

11. Late pregnancy, 6 cases: These patients were admitted for false labor, but the contractions had stopped at the time the record was obtained. All were delivered spontaneously or by low forceps after true labor had developed. The interval between the record and the onset of true labor varied from two hours to three months. This is a small group of patients on whom no other records were obtained. The absence of electrical activity in this group is similar to the findings in two other, much larger groups. In 75 patients described under "normal labor," in whom records were obtained during false labor, the electrical activity stopped when the uterine activity stopped. In the remaining 463 patients with electrical activity during labor, the electrical activity was seen *during* contractions, but not between them.

12. Electrical activity during premature separation of the placenta, 3 cases:

1. Classical picture of premature separation of the placenta in a multipara occurring at six months, with vaginal bleeding, a hard, tender uterus, constant abdominal pain, and absent fetal heart sounds. No evidence of contractions could be made out by palpation, and the patient could not detect any variation in the severity of the pain. The EHG (Fig. 4) showed bursts of irregular waves occurring every three minutes, lasting twenty to thirty seconds, at a frequency of ⅓ cycle per second and an amplitude of 200 to 350 microvolts. These are characteristic uterine waves. The cervix slowly dilated and the patient delivered eight hours later.

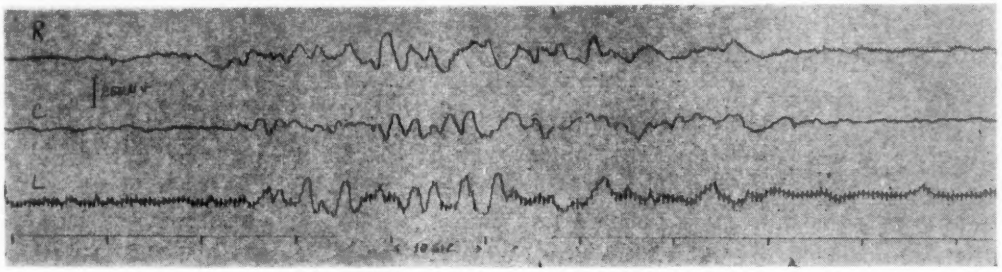

Fig. 4.—EHG recording from a case of severe premature separation of the placenta. Upper tracing *R* from right cornu, middle tracing *C* from midline of fundus, and lower tracing *L* from left cornu. Reference electrode on left flank. Calibration 250 microvolts. Time intervals 10 seconds.

2. Separation of the placenta produced by direct trauma to the uterus at eight months in a multipara, with vaginal bleeding, shock, no fetal heartbeat, and constant abdominal pain. No evidence of contractions could be made out. Recordings with the EHG over a period of 5 hours revealed *constant* electrical activity at a frequency of ½ to ⅕ cycles per second and amplitude of 50 microvolts. This patient went on to deliver spontaneously 5 minutes after the recording was completed.

3. Partial premature separation of the placenta in a multipara at term, with slight vaginal bleeding and a tender area on the uterus. The fetal heart was normal. The pa-

tient was having irregular contractions readily palpated and accompanied by backache. With each contraction characteristic uterine waves were recorded, at a frequency of ⅓ cycle per second and an amplitude of 250 to 350 microvolts. The irregular contractions continued for three days, at the end of which time she went into normal labor and delivered a living child.

13. Electrical activity during conduction anesthesia, 45 cases: These were patients receiving some form of conduction anesthesia during labor (33 caudal, 8 spinal, and 4 epidural). Characteristic uterine waves were seen in all cases. The electrical activity was weak in 14 cases, as were the uterine contractions, although the patient was in the late first stage of labor. Activity was strong in 2 cases, and moderate in 29.

In 15 cases EHG records were obtained before and after the conduction anesthesia was begun. In 7 cases the activity remained unchanged, in 6 it became weaker, and in 2 it became stronger.

Comment

Electrical activity of a characteristic type, at a frequency of ⅕ to 2 cycles per second, is found to be associated with uterine contractions, except when primary uterine inertia is present. This activity is not seen between labor contractions, or during pregnancy when the uterus is not contracting. It is seen in false as well as true labor, and it appears to be the result of normal uterine muscle activity. This activity persists during conduction anesthesia. It is also seen in cases of premature separation of the placenta.

Absence of the characteristic electrical activity *during contractions* is abnormal. Such cases are few, but cervical dilation does not occur spontaneously in them, and stimulation by Pitocin infusion does not produce dilation. These appear to be cases of true primary uterine inertia.

Most of the clinically diagnosed cases of uterine inertia were shown to have normal electrical activity. This was either weak or moderate in strength (never strong) and all such patients were delivered from below after supportive treatment and the passage of time, or after stimulation by Pitocin infusion.

These findings indicate that uterine muscle activity is normal in the great majority of cases, and that a serious abnormality of muscle function, so-called primary uterine inertia, is rare. Normal uterine action can therefore be anticipated in most cases. The final outcome of labor will be dependent upon uterine muscle action and upon the degree of disproportion present. A consideration of this group of cases on this combined basis is presented in Part II of this study.

Summary

1. The electrical activity of the human uterus was studied by means of the Electrohysterograph, with electrodes placed on the abdominal wall, in 556 cases of normal and abnormal labor.

2. The types of electrical activity found in various types of labor are described.

3. Absence of electrical activity during uterine contractions is associated with true uterine inertia. These cases are rare.

PART II. OUTCOME OF LABOR RELATED TO THE ELECTRICAL ACTIVITY OF THE UTERUS AND THE DEGREE OF DISPROPORTION

In Part I of this study the electrical activity associated with uterine contractions in 556 cases was described, the cases being divided into 12 groups according to certain clinical and x-ray criteria (see Table I). The outcome of labor in 9 of these groups, comprising 469 cases studied during the final labor, is presented in Table VI. Details of labor and degree of disproportion are given in the text of Part I under the corresponding group numbers.

TABLE VI. OUTCOME OF LABOR ASSOCIATED WITH STRENGTH OF ELECTRICAL ACTIVITY IN VARIOUS TYPES OF CASES

TYPE OF CASE	METHOD OF DELIVERY														
	SPONTANEOUS OR LOW FORCEPS WITH ELECTRICAL ACTIVITY					MIDFORCEPS WITH ELECTRICAL ACTIVITY					CESAREAN SECTION WITH ELECTRICAL ACTIVITY				
	STRONG	MODERATE	WEAK	ABSENT	TOTAL	STRONG	MODERATE	WEAK	ABSENT	TOTAL	STRONG	MODERATE	WEAK	ABSENT	TOTAL
1. Normal labor	38	220	52	0	310	0	0	0	0	0	0	0	0	0	0
2. Disproportion without inertia or Pitocin	4	7	0	0	11	1	3	0	0	4	0	13	16	0	29
3. Uterine inertia without disproportion and without Pitocin	0	2	1	0	3	0	1	0	0	1	0	0	0	2	2
4. Uterine inertia with disproportion and without Pitocin	0	0	0	0	0	0	1	0	0	1	0	1	2	1	4
5. Uterine inertia without disproportion with Pitocin	0	11	8	0	19	0	3	0	0	3	0	2	1	1	4
6. Disproportion without inertia with Pitocin	0	3	0	0	3	0	0	1	0	1	0	3	1	0	4
7. Uterine inertia with disproportion with Pitocin	0	3	2	0	5	0	1	2	0	3	0	2	3	1	6
8. Pitocin infusion for induction of labor, successful	0	34	8	0	42	0	0	0	0	0	0	0	0	0	0
9. Pitocin infusion for slow labor	0	10	4	0	14	0	0	0	0	0	0	0	0	0	0
Total	42	290	75	0	407	1	9	3	0	13	0	21	23	5	49

These cases may be grouped according to strength of electrical activity alone, without regard to the degree of disproportion or the use of Pitocin. When this is done (Table VII) it is seen that spontaneous or midforceps delivery took place in 420 cases, and cesarean section was required in 49 cases. Strong electrical activity was seen in 43, or 10 per cent, of the cases with delivery from below. None of the patients who required cesarean section showed strong activity. Moderate activity was seen in 299, or 71 per cent, of the cases of spontaneous or midforceps delivery, and in 21, or 43 per cent, of the cases which required cesarean section. Weak activity was seen in 78, or 19 per cent, of those delivered from below, and in 23, or 47 per cent, of those delivered by

cesarean section. Finally, electrical activity was absent in none of the cases of delivery from below, but was absent in 5, or 10 per cent, of the cases of cesarean section. It appears from Table VII that delivery from below is associated with stronger electrical activity, in general, than is cesarean section. Conversely, the stronger the electrical activity, the more likely is delivery to occur from below. It may be noted here that this impression was very striking in those patients with disproportion who received Pitocin infusions. Strengthening of the labor overcame degrees of disproportion which could not be overcome by the natural contractions. This strengthening, it should also be noted, resulted in death to the child from birth trauma in 2 cases.

TABLE VII. METHOD OF DELIVERY RELATED TO STRENGTH OF UTERINE ACTIVITY

METHOD OF DELIVERY	STRENGTH OF ELECTRICAL ACTIVITY								TOTAL
	STRONG		MODERATE		WEAK		ABSENT		
	NO.	%	NO.	%	NO.	%	NO.	%	
Spontaneous or low forceps	42		291		74		0		407
Midforceps	1		8		4				13
Total	43	10	299	71	78	19	0	0	420
Cesarean section	0	0	21	43	23	47	5	10	49

In Table VIII the cases are grouped according to degree of disproportion, as well as strength of electrical activity. It is seen that ease of delivery is directly correlated with the degree of disproportion, the great majority of patients with no disproportion having spontaneous or low forceps deliveries, while the great majority of those with disproportion required midforceps or cesarean section. The six patients with no disproportion who required cesarean section are noteworthy, in that 3 had no electrical activity during contractions, and hence had true uterine inertia. The remaining 3 cases were complicated by still other factors. In the group with moderate disproportion there are 2

TABLE VIII. METHOD OF DELIVERY RELATED TO DEGREE OF DISPROPORTION AND STRENGTH OF UTERINE ACTIVITY

METHOD OF DELIVERY	DEGREE OF DISPROPORTION															TOTAL
	NONE					MODERATE					SEVERE					
	ELECTRICAL ACTIVITY					ELECTRICAL ACTIVITY					ELECTRICAL ACTIVITY					
	STRONG	MODERATE	WEAK	ABSENT	TOTAL	STRONG	MODERATE	WEAK	ABSENT	TOTAL	STRONG	MODERATE	WEAK	ABSENT	TOTAL	
Spontaneous or low forceps	38	278	73	0	389	4	10	2	0	16	0	2*	0	0	2	407
Midforceps	0	0	1	0	1	1	7	3	0	11	0	1	0	0	1	13
Cesarean section	0	2†	1‡	3	6	0	4	6	2	12	0	16	15	0	31	49
Total	38	280	75	3	396	5	21	11	2	39	0	19	15	0	34	469

*One case of breech delivery and one of severe disproportion, both forced through with Pitocin infusion, both resulting in fetal death.

†One case of twins and one of breech presentation in primipara.

‡One case of prolonged inertia due to caudal anesthesia.

who also showed no electrical activity. Thus of the 49 patients who required cesarean section, a total of 43 had demonstrable disproportion, while 5 had true primary uterine inertia.

Summarizing the tables and referring to the cases as described in Part I, it is possible to make the following general statements:

1. When cephalopelvic disproportion was absent, delivery from below was accomplished successfully in 389 cases, *all* of which showed characteristic uterine electrical activity present in some degree. Cesarean section was necessary in 3 cases, *none* of which showed characteristic uterine electrical activity, and in 3 cases with additional complicating factors.

2. When cephalopelvic disproportion was present, the method of delivery was related directly to the degree of disproportion, *if normal electrical activity was present and Pitocin was not given* (48 cases).

3. When disproportion was present, together with normal electrical activity, and Pitocin was used, the outcome of labor still depended primarily upon the degree of disproportion, but it was possible to overcome higher degrees of disproportion under these circumstances (27 cases). Death from birth injury resulted in 2 of these cases.

4. When normal electrical activity was absent during labor, cesarean section was necessary. The absence of disproportion and the use of Pitocin did not influence this (5 cases).

Comment

Study of uterine muscle activity by means of the Electrohysterograph has shown that such activity is nearly always of a normal type, in the sense that dilation of the cervix will eventually result. Such activity varies considerably in strength, and the speed of dilation varies correspondingly. When this activity is slow, it can be stimulated by the use of Pitocin. Disproportion influences the outcome of labor by mechanical means. The type of electrical activity associated with labor is not directly influenced by the presence or absence of disproportion, but delivery from below results only when the strength of uterine activity is great enough to overcome the disproportion present.

It is worth while, therefore, to estimate by x-ray pelvimetry the degree of disproportion present in any case which is not progressing normally. The probability of delivery from below can then be determined. It is also useful to study the uterine activity, for, if disproportion is absent, and uterine activity is normal, delivery from below will result in time, or the labor can be stimulated by Pitocin. When disproportion exists, strong labor will overcome it, but occasionally at great risk to the child. Strong labor which occurs spontaneously may therefore be dangerous, and strong labor should never be produced by Pitocin stimulation in the presence of disproportion.

When normal electrical activity is absent, the cervix does not dilate normally, and delivery from below will not occur even when disproportion is ab-

sent. Such cases will not respond to Pitocin stimulation. These cases can be discovered by the Electrohysterograph. They can also be discovered by a trial of Pitocin by infusion (x-rays having shown *no disproportion*).

Summary

1. The outcome of labor has been correlated with the electrical activity of the uterus and with the degree of disproportion in 469 cases.

2. In general, the stronger the electrical activity of the uterus the more likely is delivery from below.

3. Ease of delivery from below is related to the degree of disproportion.

4. When normal electrical activity is absent, delivery from below will not occur, even with Pitocin infusion, regardless of the presence or absence of disproportion.

PART III. UTERINE INERTIA

In Parts I and II of this study, the electrical activity associated with uterine contractions in 556 cases was described. This activity was correlated with the clinical impression of the labor, with the type of delivery, and with the presence of disproportion. In this group, there were 51 cases in which a clinical diagnosis of uterine inertia was made, and these are considered together in this Part of the study.

Material and Methods

All patients were studied in the Labor Rooms of the Sloane Hospital for Women. A recording of the electrical activity associated with uterine contractions was made in each case. These records were analyzed according to the method described in Part I. Roentgen pelvimetry was performed in all cases in which disproportion was suspected.

Selection of the 51 cases described in this Part of the study was on the basis of a clinical diagnosis of uterine inertia. This diagnosis was based on failure of the cervix to dilate, with the strength and frequency of contractions either remaining unchanged or becoming weaker. Emphasis is laid upon the *clinical* nature of this diagnosis, because in each case those responsible for management were impressed by failure of the patient to show progress. The purpose of the study was to determine whether these cases were all of the same type, or whether some points of differentiation could be discovered which would indicate different methods of treatment.

These were all cases of so-called "primary" uterine inertia, except for 3 cases in which the inertia was produced by caudal anesthesia. There were no cases of "secondary" inertia in the series, other than the 3 secondary to caudal anesthesia. There were 49 primiparas and 2 multiparas. One multipara was felt to have inertia, although she progressed very slowly and delivered without Pitocin. The other multipara had an oblique lie and never developed good labor. The length of labor varied from fifteen to one hundred twenty hours, with a mean and a median of thirty-five hours. The cases were divided into groups according to the presence or absence of disproportion, and according to whether or not Pitocin was used.

Results

The results are tabulated according to the various groups (Tables IX to XII). The details of the cases are given in Part I of the study.

The strength of the electrical activity in each of the groups is shown in Table XIII. The significant finding is that electrical activity was *present* in 46 cases (Fig. 5), and *absent* in 5 cases (Figs. 6 to 8). This indicates, on the basis of the findings in Part I of this study, that normal uterine muscle activity was present in 46, or 90 per cent, of these cases of uterine inertia. The 5 who

TABLE IX. UTERINE INERTIA, WITHOUT DISPROPORTION, WITHOUT PITOCIN (GROUP 3 IN PART I)

METHOD OF DELIVERY	NO.	PARITY	ELECTRICAL ACTIVITY	DEGREE OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN
Spontaneous or low forceps	3	Primipara	Moderate	None	30	None
		Primipara	Moderate	None	37	None
		Multipara	Weak	None	15	None
Midforceps	1	Primipara	Weak	None	24	None
Cesarean section	2	Primipara	None	None	16	None
		Primipara	None	None	22	None
Total	6					

Mean duration of labor: all cases, 24 hours; delivered from below, 26½ hours; cesarean section, 19 hours.

TABLE X. UTERINE INERTIA, WITHOUT DISPROPORTION, WITH PITOCIN (GROUP 5 IN PART I)

METHOD OF DELIVERY	NO.	PARITY	ELECTRICAL ACTIVITY	DEGREE OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN
Spontaneous or low forceps	19	Primipara	Moderate	None	40	1½
		Primipara	Moderate	None	60	18½
		Primipara	Moderate	None	38	5
		Primipara	Moderate	None	32	3½
		Primipara	Moderate	None	44	4
		Primipara	Moderate	None	42	7
		Primipara	Moderate	None	39	8
		Primipara	Moderate	None	30	⅔
		Primipara	Moderate	None	28	10
		Primipara	Moderate	None	28	3
		Primipara	Moderate	None	25	4
		Primipara	Weak	None	30	2½
		Primipara	Weak	None	50	3
		Primipara	Weak	None	25	2½
		Primipara	Weak	None	32	1½
		Primipara	Weak	None	48	1¼
		Primipara	Weak	None	28	5
		Primipara	Weak	None	26	2
		Primipara	Weak	None	35	1¼
Midforceps	3	Primipara	Moderate	None	30	7
		Primipara	Moderate	None	26	1 caudal
		Primipara	Weak	None	24	7
Cesarean section	4	Primipara	Moderate	Breech	15	2
		Primipara	Moderate	Twins	32	18
		Primipara	Weak	None	34	14 caudal
		Primipara	None	None	23	4
Total	26					

Mean duration of labor: all cases, 33 hours; delivered from below, 34½ hours; cesarean section, 26 hours.

Mean duration of Pitocin infusion: all cases, 5.3 hours; delivered from below 4.5 hours; cesarean section 9.5 hours.

did not have demonstrable electrical activity during labor all required cesarean section. Two of them were treated with Pitocin (for 4 hours in each case) while 3 received no Pitocin. These are probably the only cases of true primary uterine inertia in this study, the others representing slow, but normal labor.

TABLE XI. UTERINE INERTIA, WITH DISPROPORTION, WITHOUT PITOCIN (GROUP 4 IN PART I)

METHOD OF DELIVERY	NO.	PARITY	ELECTRICAL ACTIVITY	DEGREE OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN
Spontaneous or low forceps	0					
Midforceps	1	Primipara	Moderate	Moderate, in midpelvis	29	None
Cesarean section	4	Primipara	Moderate	Severe, in midpelvis	36	None
		Primipara	Weak	Moderate at inlet (difference 1.3 cm.)	21	None
		Multipara	Weak	Severe (oblique lie)	86	None
		Primipara	None	Moderate, in midpelvis	25	None

Mean duration of labor: all cases, 39½ hours; delivered from below, 29 hours; cesarean section, 42 hours.

TABLE XII. UTERINE INERTIA, WITH DISPROPORTION, AND WITH PITOCIN (GROUP 7 IN PART I)

METHOD OF DELIVERY	NO.	PARITY	ELECTRICAL ACTIVITY	DEGREE OF DISPROPORTION	LENGTH OF LABOR (HOURS)	HOURS OF PITOCIN
Spontaneous or low forceps	5	Primipara	Moderate	Moderate at inlet (difference 1.6 cm.)	28	9
		Primipara	Moderate	Moderate at inlet (difference 1.2 cm.)	37	2
		Primipara	Moderate	Severe at inlet (neonatal death) (difference 1.0 cm.)	48	5
		Primipara	Weak	Moderate at inlet (difference 1.5 cm.)	22	6
		Primipara	Weak	Moderate in midpelvis	15	2
Midforceps	3	Primipara	Moderate	Moderate at inlet (difference 1.6 cm.)	61	13
		Primipara	Weak	Moderate at inlet (difference 1.7 cm.)	36	½
		Primipara	Weak	Severe at midpelvis	18	6
Cesarean section	6	Primipara	Moderate	Severe at inlet (difference 1.1 cm.)	24	2
		Primipara	Moderate	Severe in midpelvis	64	10½
		Primipara	Weak	Moderate in midpelvis	120	3
		Primipara	Weak	Moderate in midpelvis	37	5
		Primipara	Weak	Moderate at inlet (difference 1.3 cm.)	36	8
		Primipara	None	Moderate at inlet (difference 1.7 cm.)	23	4
Total	14					

Mean duration of labor: all cases, 41 hours; delivered from below, 33 hours; cesarean section, 51 hours.

Mean duration of Pitocin infusion: all cases, 5.4 hours; delivered from below, 5.4 hours; cesarean section, 5.4 hours.

Disproportion was present in 19 cases (37 per cent) of this group. Electrical activity was present in 17 of these cases and was of the same strength as seen in those cases without disproportion. Apparently disproportion of itself does not influence uterine activity. The presence of disproportion in these cases is significant, however, in that it may be more important than the inertia in obstructing the labor. Furthermore, stimulation with Pitocin in the presence of unrecognized disproportion may overcome the disproportion at the cost of damage to the infant.

It appears, then, that clinical uterine inertia represents slow labor in 90 per cent of the cases. There is a significant degree of disproportion present in 37 per cent. True uterine inertia which will not respond to treatment by rest or stimulation is present in 10 per cent, whether disproportion exists or not.

The outcome of labor in the entire group is correlated with the degree of disproportion and the presence or absence of electrical activity in Table XIV.

TABLE XIII. STRENGTH OF ELECTRICAL ACTIVITY IN UTERINE INERTIA

	ELECTRICAL ACTIVITY				
	STRONG	MODERATE	WEAK	ABSENT	TOTAL
1. Uterine inertia, without disproportion, without Pitocin	0	2	2	2	6
2. Uterine inertia, without disproportion, with Pitocin	0	15	10	1	26
3. Uterine inertia, with disproportion, without Pitocin	0	2	2	1	5
4. Uterine inertia, with disproportion, with Pitocin	0	6	7	1	14
Total	0	25	21	5	51

TABLE XIV. OUTCOME OF LABOR RELATED TO DEGREE OF DISPROPORTION AND STRENGTH OF ELECTRICAL ACTIVITY

	DEGREE OF DISPROPORTION						
	SEVERE		MODERATE		NONE		
	ELECTRICAL ACTIVITY		ELECTRICAL ACTIVITY		ELECTRICAL ACTIVITY		
METHOD OF DELIVERY	PRESENT	ABSENT	PRESENT	ABSENT	PRESENT	ABSENT	TOTAL
Spontaneous or low forceps	1*	0	4	0	22	0	27
Midforceps	1	0	3	0	4	0	8
Cesarean section	4	0	4	2	3†	3	16
Total	6	0	11	2	29	3	51

*Neonatal death.

†One breech presentation, one case of twins, and one case of prolonged inertia due to caudal anesthesia.

There were 27 patients who were delivered spontaneously or by low forceps. All of these had electrical activity of weak or moderate strength. There was no disproportion in 22, and moderate disproportion in 4. In one case severe disproportion was present, with a difference between the diameter of the inlet circle and the biparietal diameter of the fetal head of only 1.0 cm. This patient was delivered by low forceps, after a Pitocin infusion of five hours. The severe degree of disproportion was overcome, but the child died a few hours after birth of intracranial injury.

There were 8 patients who were delivered by midforceps. Four of these had disproportion, and 4 did not. All of these cases showed electrical activity. There were thus a total of 35 cases of delivery from below, all of which showed electrical activity.

There were 16 patients who required cesarean section. Five of these showed no electrical activity, and 2 of these 5 had disproportion in addition. Four patients had severe degrees, and 4 had moderate degrees of disproportion. All of these showed electrical activity. Three others also had cesarean section, with electrical activity present, after Pitocin infusion. One of these was a primipara with a breech presentation, another was a primipara with twins, and a third had severe and prolonged inertia due to caudal anesthesia.

The mean length of labor was thirty-nine hours in those cases requiring cesarean section and thirty-three hours in those with delivery from below. This indicates that the decision for cesarean section was made, on the average, after sufficient time had elapsed for delivery from below to take place.

Pitocin was used in a total of 40 cases. Thirty of these patients were delivered from below, the Pitocin helping to overcome disproportion in 8 of them. Electrical activity was present in all of these cases. Cesarean section was required in 10 cases. Two of these had no electrical activity. Electrical activity was present in the remaining 8, but 5 of these had disproportion, and the remaining 3 were complicated by other factors (see footnote to Table XIV).

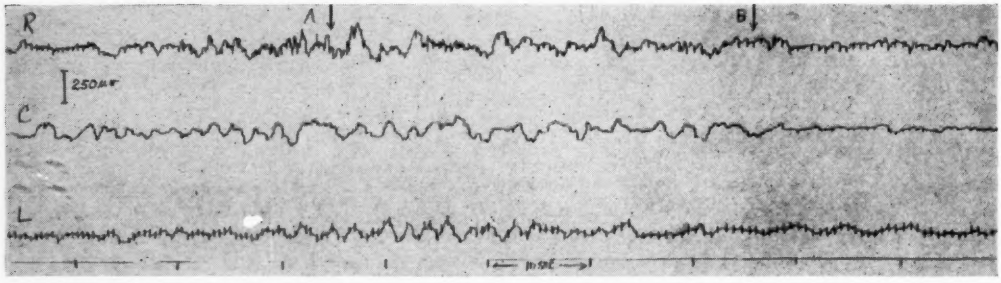

Fig. 5.—Electrohysterograph recording from a primipara with clinical uterine inertia. Total labor, twenty-four and one-half hours. Cervix a rim for three hours at time of record shown. After another hour, cervix was pushed back manually and child delivered easily by midforceps.

Upper tracing *R* from electrodes over right cornu, middle tracing *C* from electrodes over fundus, and lower tracing *L* from electrodes over left cornu. Time interval 10 seconds. Calibration 250 microvolts. Pain as felt by patient began at *A* and ended at *B*.

Electrical activity began before *A*, and ends near *B*. Electrical activity is of greatest duration at *C*, less at *R*, and least at *L*. This is a record of "weak" strength, the waves being of normal pattern. This type of activity represents weak, slow uterine action. It can be stimulated with Pitocin, but Pitocin was not used in this case.

Pitocin was used in two groups. There was a wide variation in the length of time during which Pitocin was given, as shown in Tables X and XII. In the group with inertia but without disproportion (26 cases) the mean duration of Pitocin infusion was 5.3 hours. In those delivered from below the mean was 4.5 hours, while in those who required cesarean section the mean was 9.5 hours. Those who required cesarean section were thus treated well beyond the time at which delivery usually occurred in the group delivered from below. When disproportion was present (14 cases) the mean duration of Pitocin infusion was 5.4 hours, whether delivery from below was performed or not. In this group the disproportion was an important factor, so that use of Pitocin was not prolonged.

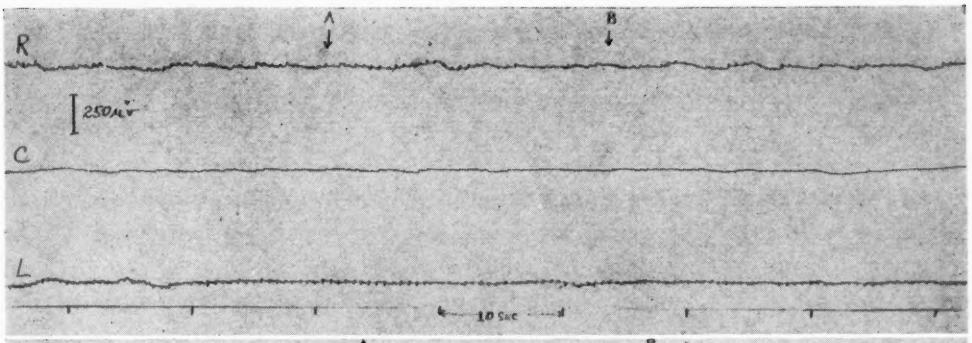

Fig. 6.

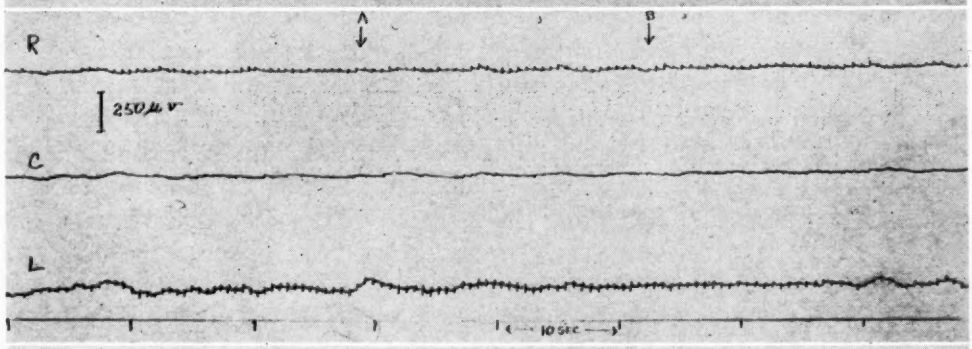

Fig. 7.

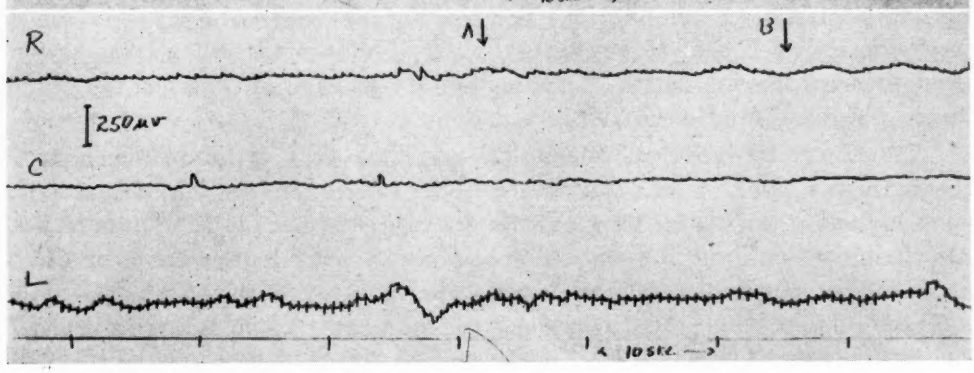

Fig. 8.

Figs. 6, 7, and 8.—Electrohysterograph record from a primipara with true primary uterine inertia. Upper tracing *R* from electrodes over right cornu, middle tracing *C* from electrodes over fundus, and lower tracing *L* from electrodes over left cornu. Time interval 10 seconds. Calibration 250 microvolts.

Labor lasted thirty-four and one-half hours, membranes having ruptured spontaneously two hours before the onset of labor. Pains mild and irregular, at three- to seven-minute intervals, lasting thirty to fifty seconds, for first twenty-six hours. At the end of twenty-six hours, the record shown in Fig. 6 was obtained. Pain, as felt by the patient, began at *A* and ended at *B*. The uterus became moderately hard during this time. There is no evidence of uterine electrical activity at any time.

A Pitocin infusion was then begun, and at twenty-eight and one-half hours of labor the record shown in Fig. 7 was obtained. At this time contractions were occurring every one and one-half to two and one-half minutes, with pain so severe caudal anesthesia had just been started. Again, pain, as felt by the patient, began at *A* and ended at *B*. The uterus hardened at this time. No uterine electrical activity is seen.

The infusion was continued, and at thirty hours of labor the record shown in Fig. 8 was obtained. The Pitocin infusion was running at 50 drops per minute. Contractions were occurring every two minutes, lasting forty seconds. Pain was so severe that caudal anesthesia at level T_{10} did not control it. Pain, as felt by the patient, began at *A* and ended at *B*. There is no evidence of uterine electrical activity.

The cervix was a tight 2 fingers' dilated at twenty-four hours of labor and never changed thereafter. A cesarean section was performed after thirty-four and one-half hours of labor.

This record is marked by total absence of normal uterine waves. This type of case will not respond, clinically or electrically, to a Pitocin infusion.

Pitocin was not used in 11 cases. Delivery from below was carried out in 5 cases, all of which showed electrical activity. Cesarean section was required in 6 cases. Three of these showed no electrical activity. The remaining 3 showed electrical activity and had disproportion in addition.

Comment

In this series of 51 cases diagnosed clinically as "primary uterine inertia," electrical activity of the normal type was found to be present in 46, or 90 per cent, of the cases. Those cases with normal electrical activity were delivered from below (35 cases) unless disproportion was present to such degree that cesarean section was warranted (11 cases). Pitocin stimulated the labor successfully in 30 of the 35 cases delivered from below, and the remaining 5 were delivered without such stimulation. In the 11 cases requiring cesarean section, Pitocin also stimulated the contractions successfully in 8. Since all of these patients either achieved full dilation and were delivered from below or were delivered by cesarean section because of mechanical factors, it is felt that these 46 cases represent uterine activity of a normal type, that is, they had *slow, normal* labor.

There were 5 patients with no electrical activity, 2 of whom received Pitocin. None of these achieved more than 2 fingers' dilation, and all of them required cesarean section. On the basis of the findings with the Electrohysterograph, it is felt that these represent a true abnormality of uterine action, a true primary uterine inertia, since neither the passage of time nor the use of Pitocin produced dilation of the cervix.

The Electrohysterograph thus differentiates two types of "primary" uterine inertia, one in which electrical activity of the type seen in normal labor is found, and one in which no electrical activity is found on the abdominal wall during uterine contractions. The first type represents normal labor which is proceeding more slowly than usual. The total duration of labor will be more than twenty-four hours in most of these cases, but full dilation will eventually occur if enough time is allowed to elapse and the patient is adequately supported. Pitocin by infusion will effectively stimulate the uterus in such cases and thereby shorten the labor.

The second type of uterine inertia represents a basic disturbance of uterine-muscle activity. Prolonged labor, with adequate support of the patient, will not produce dilation. Pitocin infusion will not produce dilation. The uterine muscle, although contracting, does not provide sufficient force, and such force cannot be provided even with Pitocin.

This suggests two possibilities. It may be that an abnormality exists within the uterine muscle fiber such that a contraction of the fiber (whether spontaneous or Pitocin stimulated) always produces less than the required amount of force. This would represent abnormality in the contractile apparatus within the fiber. This apparatus consists of the proteins actin and myosin, together with their combined form actomyosin. The physical properties of the actin-myosin-actomyosin system depend upon the amount of these

substances present, and upon the ratio of myosin to actomyosin. Csapo[5] has shown that the amount of myosin plus actomyosin and the ratio of myosin to actomyosin increase during pregnancy, reaching their highest amounts in labor. These amounts are also increased by administration of estrogens.[6] It is possible that labor may occur, in occasional instances, with the contractile mechanism in less than the ideal condition for labor.

The second possibility has to do with the transmission of the impulse to contract. This was previously discussed[1] as an explanation for the absence of electrical activity in true uterine inertia. Groups of uterine muscle fibers act together as a functional syncytium. The reactivity of these fibers depends on the presence of estrogens (among other substances), and variation of reactivity depends upon transmission of the electrical impulse over large or small numbers of these fibers. If a large number of fibers react as a unit, a large electrical wave will be produced, and a large mechanical force will be exerted. If only a small group of fibers react as a unit, the electrical waves produced will be too small to be recorded from the abdominal wall, and the resulting mechanical force will be too small to dilate the cervix. Further work is necessary in order to clarify the basic cause of this disorder.

True uterine inertia can also be differentiated from slow, but normal, labor by a trial of Pitocin infusion. When true primary inertia is present, Pitocin *will not* produce cervical dilation. When the labor is normal, though slow, Pitocin *will* produce cervical dilation. The length of trial with Pitocin cannot be stated in round figures, since progress may be fast or slow. In those cases successfully treated with Pitocin the range of duration of the infusion varied from one-half hour to eighteen and one-half hours. The mean duration of the infusion was 4.8 hours, and the median was four hours. This would suggest that a trial of Pitocin for five hours is probably adequate to produce progress if any progress is to be produced.* If no progress is found, cesarean section should be performed. If progress occurs, the infusion should be continued through delivery.

This type of study finally resolves itself into a theoretical and a practical aspect. The theoretical aspect has to do with the intimate nature of uterine muscle contraction and its abnormalities. This may be approached by means of the Electrohysterograph, which will predict the type of labor to be expected as time goes on, but it may also be approached by the use of a Pitocin infusion. The Electrohysterograph possesses the advantage that those cases in which Pitocin fails can be selected without subjecting the patient to additional labor. Most patients can readily tolerate an additional five hours of labor, however, and hence from a practical point of view the Pitocin may be used diagnostically as well as therapeutically.

Summary

1. The electrical activity of the uterus and the degree of disproportion were studied in 51 cases of clinical uterine inertia.

*This, of course, means that the speed of the infusion be so adjusted that contractions occur at intervals of not less than three minutes.

2. Uterine inertia represents slow but normal labor in 90 per cent of these cases.

3. Primary uterine inertia, a true disorder of uterine muscle function, is present in 10 per cent of these cases.

4. True primary uterine inertia will not respond to supportive therapy or to Pitocin stimulation.

5. The differentiation between true primary uterine inertia and slow, normal labor can be made early by means of the Electrohysterograph, and can be made by a trial of Pitocin infusion.

6. The possible nature of the basic disorder in primary uterine inertia is discussed.

References

1. Steer, C. M., and Hertsch, G. J.: AM. J. OBST. & GYNEC. 59: 25, 1950.
2. Halliday, E. C., and Heyns, O. S.: J. Obst. & Gynaec. Brit. Emp. 59: 309, 1952.
3. Levy-Solal, E., Morin, P., and Zacouto, F.: Presse méd. 60: 1335, 1952.
4. Moloy, H. C., and Steer, C. M.: AM. J. OBST. & GYNEC. 60: 1135, 1950.
5. Csapo, A.: Am. J. Physiol. 160: 46, 1950.
6. Csapo, A.: Am. J. Physiol. 162: 406, 1950.

ESTIMATION OF FETAL WEIGHT USING LONGITUDINAL MENSURATION

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ESTIMATION of fetal weight in utero has become increasingly important in regard to the prevention of prematurity, and in evaluation of fetopelvic proportion in those instances where a large baby is suspected and pelvimetry is being considered or has been obtained.

Survival of the premature infant has been shown to be related more to fetal weight than to any other consideration.[1] The obstetrician is faced with estimation of the fetal weight when interruption of pregnancy is considered at a relatively elective time. These occasions arise with conservative management of placenta previa, repeat cesarean section, interruption of pregnancy in the treatment of toxemia and diabetes, and, in some communities, the practice of induction for convenience.

X-ray pelvimetry in millimeters with its admitted accuracy appears to be ridiculous without due regard to the size of the infant. Donaldson and Cheney[2] proved the accuracy of x-ray fetal cephalometry to be equal to that of pelvimetry, but in the same study they showed that differences in muscular, skeletal, and fatty development reduced the accuracy of their birth weight predictions to only 36 per cent within 8 ounces. The high incidence of birth trauma in large babies, reported by Nathanson[3] to be 3.5 per cent, may be largely attributed to these differences between the size of the head and the size of the body.

Poulos and Langstadt,[4] recognizing the inaccuracy of x-ray estimations of fetal weight, developed a volumetric method based on external transverse and longitudinal measurements with the pelvimeter. The abdominal wall thickness and station were taken into consideration, and the longitudinal diameter was sometimes obtained with one finger in the rectum. Unusual presentations and positions were not considered in their series. Two graphs were plotted from 21 vertex presentations, all of which were at minus stations. Sixty-eight per cent of the birth weights were determined statistically to fall within ± 230 grams by one method or ± 250 grams by another method in this selected group. Since a considerable amount of calculation is necessary, the graph seems to be an important part of the method.

Method

McDonald's measurement of the height of the fundus from the upper edge of the symphysis pubis following the curvature of the abdomen with a tape measure was determined in 200 pregnancies. Measurements were made during uterine relaxation if the patients were in labor. The upper hand was placed

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firmly against the top of the fundus with the measuring tape passing between the index and middle fingers. Readings were taken from the perpendicular intersection of the tape with the fingers. Since the tape followed the curvature of the abdomen, it is believed that this single measurement partially represents changes in volume as well as length. Measurements including rectal examination for determination of station of the presenting part were made by one of us (R. J.) in the majority of instances. If these measurements were recorded within one week of delivery, they were included in the series. Crown-rump lengths using the tape measure were substituted for McDonald's measurement when oblique or transverse presentations were encountered or the presenting part was above the symphysis, and the station was considered to be a minus station. Only twin pregnancies were deleted from the series. Many of these were measured by request in problem cases.

Certain inherent errors such as hydramnios, site of the placenta, and molding of the head are obvious; the degree cannot be ascertained by the method, and they were therefore ignored. Other factors such as station, parity, condition of the membranes, obesity, and position were found to be available for statistical investigation.

An arbitrary formula was developed assuming that the height of the fundus at station zero should be 35 cm. with an average-sized baby at term weighing 7 pounds, 8 ounces. The spines were made a fixed point of reference with the station to be analyzed for possible influence in results. The station zero group was studied first to find a mean ounces per centimeter variation in the birth weight depending solely on the abdominal measurement. The other groups according to station were then compared with the station zero group for evidence of a constant and, therefore, correctable error in estimation. With the influence of station thus determined, as explained under results below, the assumed formula was established as follows:

$$W = 7 \text{ pounds, } 8 \text{ ounces} + [(M + S - 35 \text{ cm.}) \ (5 \text{ ounces})]$$

The mean ounces per centimeter deviation from the assumed mean of 5 ounces per centimeter was then statistically determined, and the other variables mentioned in the preceding paragraph were evaluated by comparison with the formula containing the true mean.

TABLE I. PARITY, PRESENTATION, AND PROGRESS OF LABOR

VARIABLES	STATION						TOTAL	PERCENTAGE
	FLOATING	−3	−2	−1	0	+1		
A. Parity.—								
Nulliparous	1	3	8	14	19	11	56	28.0
Parous	8	17	32	36	41	10	144	72.0
B. Presentation.—								
Vertex	5	18	39	50	58	21	191	95.5
OA	4	7	20	26	30	13	100	50.0
OP	0	4	10	10	10	7	41	20.5
OT	1	5	6	12	15	0	39	19.5
Undetermined	0	2	3	2	3	1	11	5.5
Breech	2	2	1	0	2	0	7	3.5
Transverse	2	0	0	0	0	0	2	1.0
C. Membranes.—								
Intact	8	14	30	38	44	13	147	73.5
Nulliparous	0	2	6	11	14	8	41	20.5
Parous	8	12	24	27	30	5	106	53.0
Ruptured	1	6	10	12	16	8	53	26.5
Nulliparous	1	1	2	3	5	3	15	7.5
Parous	0	5	8	9	11	5	38	19.0

Results

Table I presents the station, parity, presentation and position, and condition of the membranes in the 200 pregnancies studied. Only 28 per cent were nulliparous. There were 95.5 per cent vertex, 3.5 per cent breech, and 1 per cent transverse presentations. There were no face presentations. The frequency of these presentations corresponds well with that reported by Eastman[5] in the first 7,500 admissions to the Johns Hopkins obstetrical service—94.6 per cent, 3.9 per cent, and 0.96 per cent, respectively.

1. Station.—The station in centimeters was subtracted from the abdominal measurement if they were minus stations and added if they were plus stations

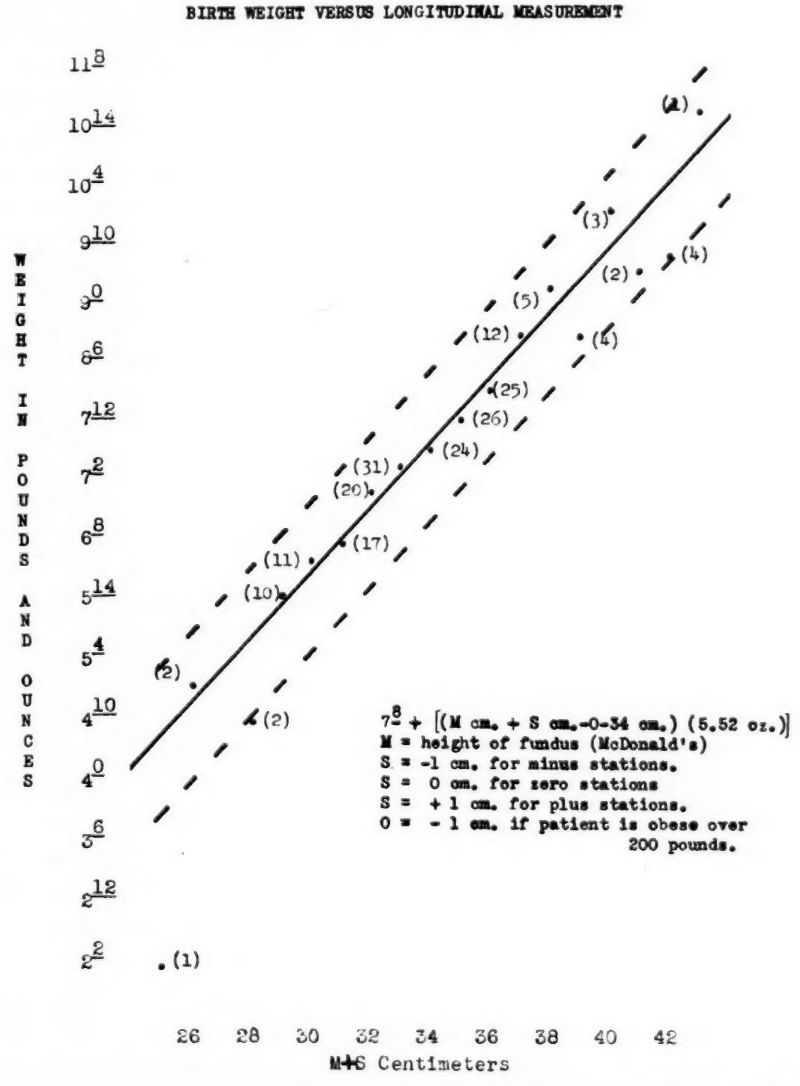

Fig. 1.—Statistically determined mean, 200 cases (solid line), standard deviation (broken lines), and actual birth weight means for each factor of M + S (dots with the number of cases in parentheses).

since it was probable that the fundus follows the baby downward during descent to some extent. The results obtained indicated that this is only partially true. If nothing were subtracted for minus stations, the babies in this group weighed less than the estimated weight derived from similar measurements in the station zero group. However, if more than 1 cm. were subtracted for any of the minus stations, the actual birth weight was more than the estimated weight. We found that by subtracting only 1 cm. from the abdominal measurement if the station was above the spines, the estimated results were as good as the station zero group. Results were similarly improved by adding 1 cm. to the abdominal measurement if the station was below the spines.

Fig. 1 shows the statistically determined mean for the 200 cases studied (solid line), the standard deviation (broken lines), and the means of the actual weights observed (dots with the number of cases in parentheses) for each factor of M + S. The formula expressing the mean is given in the lower right-hand corner. The convenient mid-point of 7 pounds, 8 ounces, used in the assumed formula, was found to be represented by a factor of 34 cm. rather than 35 cm., and the formula stating the statistically determined mean was changed accordingly.

One centimeter in the M + S factor represents a difference of 5.52 ounces. The mean weight of the infants in this series was 7.43 pounds.

2. Obesity.—Obesity influences this method of estimation because of the proportionately larger amount of abdominal wall thickness. Eleven women were known to weigh over 200 pounds. The mean deviation in birth weight compared with the established mean for all 200 cases was minus 5.45 ounces. Since this is so close to the ounces per centimeter mean of 5.52, correction for obesity with its increased abdominal wall thickness may simply be made by subtracting 1 cm. from the factor M + S.

3. Condition of the Membranes.—Fifty-three women were believed to have ruptured membranes at the time they were measured. The mean deviation in birth weight from the mean established for the entire group was only +0.17 ounces. Correction is therefore not necessary.

4. Position and Presentation.—No constant error was observed in the various presentations and positions comparing their mean deviations in weight with that of the whole group. The mean for the occiput posteriors was only 1.61 ounces less than the estimated weights. There were too few breech presentations for statistical analysis. Five of the seven breeches were within the standard deviation of 12.45 ounces for the total cases. The two transverse presentations were interesting since crown-rump length at a minus station was used in the estimation, and the birth weights were one ounce more and seven ounces more than the estimated weights. Recent experience since analysis of these first 200 cases was begun has indicated that, possibly due to the markedly flexed attitude of babies in a transverse presentation, they tend to weigh even more than the estimated weight.

5. Parity.—Parity was expected to influence estimation by this method because of relaxed abdominal musculature, diastasis, etc. However, the average birth weight in the nulliparous group was only 0.69 ounce less than the estimate.

Comment

Estimation of fetal weight in utero may be reduced to the following steps:

1. One centimeter is subtracted from or added to the abdominal measurement *only* if the station is above (minus) or below (plus) the spines. This is the factor M + S.

2. Another centimeter is subtracted from the above factor *only* if the patient weighs more than 200 pounds.

3. The difference between this figure and 34 centimeters is obtained and multiplied by 5½ ounces. That number of ounces is either added to or subtracted from 7 pounds, 8 ounces depending on whether the figure was more or less than 34 centimeters.

Sixty-eight per cent of all the babies weigh within 12.45 ounces of the estimate, the standard deviation. Graphs are not necessary for the estimation. The following example will show the same steps mathematically:

Height of the fundus, McDonald's measurement	M = 32 cm.
Station	S = –2 cm.
Obesity, weight over 200 pounds	O = –1 cm.

Weight = 7# + [(M + S – O – 34) (5½ ounces)]
Weight = 7# + [(32 –1 –1 –34) (5½ ounces)]
Weight = 7# + [(–4) (5½ ounces)] = [–22 ounces]
Weight = 7# + [(–22 ounces)] = 6 pounds, 2 ounces

Comparison with the volumetric method of estimation reported by Poulos and Langstadt would at first indicate that accuracy has been sacrificed for simplicity. However, since they used only 21 cases in deriving their means, their standard deviations lack significance. Using the method presented in this paper, 50.5 per cent of birth weights will be within 8 ounces or ± 240 grams compared with 68 per cent within ± 230 and ± 250 grams as reported by Poulos and Langstadt. Using a standard formula to determine the statistical significance of a difference between two sample rates, we find that the difference may be explained by chance alone 11.4 times out of 100, and we may conclude that the difference is not statistically significant.*

*Volumetric method –	21	cases,	14.28	within 8 ounces =	68.0%
Presented method –	200	cases,	101.0	within 8 ounces =	50.5%
Totals	221		115.28	Difference	17.5%

$$\frac{115.28}{221} \times 100 = 52.1\% \qquad \begin{array}{r} 100.0\% \\ -52.1\% \\ \hline 47.9\% \end{array}$$

$$SE = \sqrt{\frac{52.1 \times 47.9}{21}} = 10.89$$

$$SE = \sqrt{\frac{52.1 \times 47.9}{200}} = 3.53$$

$$SE_{(Difference)} = \sqrt{(10.89)^2 + (3.53)^2} = 11.04 \qquad \frac{17.5\%}{11.04} = 1.58$$

Integration table reveals 88.6 per cent confidence or 11.4 per cent probability by chance.

It will be noted that a factor of 26 cm. will indicate a premature weight in 84.13 per cent of the infants, while a factor of 30 cm. must be present before we have similar assurance that the baby will not be premature by weight. The

relationship between abdominal measurement and other factors and the expected incidence of an excessively large-sized infant can also be determined by reference to Fig. 1.

Summary

The height of the fundus is 34 cm. with an average-sized baby of 7 pounds, 8 ounces in utero at station zero. Measurements more or less than 34 cm. indicate a baby weighing 5½ ounces per centimeter more or less than 7½ pounds. Corrections for stations other than zero and for obesity are easily made.

1. The equation for the prediction of birth weight based on 200 cases is:
W = 7 pounds, 8 ounces + [(M + S − 0 − 34 cm.) (5.52 oz.)]
M = height of the fundus (McDonald's measurement in centimeters)
S = −1 cm. for minus stations.
S = 0 cm. for zero stations.
S = +1 cm. for plus stations.
O = −1 cm. correcting obesity, if the patient weighs over 200 pounds.

2. The standard deviation for this method is ± 12.45 ounces, or 68 per cent of all babies estimated will be within that range.

3. More complicated ways of estimating birth weight have not been proved statistically to be better than the method presented.

References

1. Taylor, H. W., and Ward, E. J.: Am. J. Obst. & Gynec. **65**: 1276, 1953.
2. Donaldson, S. W., and Cheney, W. D.: Radiology **50**: 666, 1948.
3. Nathanson, J. W.: Am. J. Obst. & Gynec. **60**: 54, 1950.
4. Poulos, P. P., and Langstadt, J. P.: Am. J. Obst. & Gynec. **65**: 233, 1953.
5. Eastman, Nicholson J.: Williams Obstetrics, ed. 10, New York, 1950, Appleton-Century-Crofts, Inc.

TUBAL LIGATION (STERILIZATION) BY A MODIFIED MADLENER METHOD

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THE term sterilization for the permanent prevention of pregnancy is an unfortunate one because one of its meanings is to castrate. The term tubal ligation is preferable, since the purpose of the operation is rarely to castrate.

Dieckmann and Hauser,[1] in 1948, reported a 3.6 per cent failure rate of tubal ligations at this hospital. The present study was an unpleasant surprise, because our incidence of pregnancies after tubal ligation was still too high. The results indicate that (1) the surgeon was careless, (2) the method was at fault, or (3) there was something atypical about the Fallopian tubes in the patient in whom pregnancy subsequently occurred. The injection of sodium morrhuate into the lumen of the tube in addition to the Madlener technique, seemed to be a valuable addition.

Dieckmann and Hauser reported 912 cases of tubal ligation; 3.6 per cent of these patients became subsequently pregnant. In all of these cases the original Madlener technique was not followed in that a Kocher or hemorrhoidal clamp was used to crush the tube instead of a Payr clamp, and the tube was crushed near the uterus instead of at the free outer third as described by Madlener.[2] Dippel[3] in 1940 suggested that most failures following the Madlener method were due to the surgeon's not following the original method but using one of the many modifications. He was able to show a break in technique in most of the failures. Knight[4] in 1946 collected 4,952 cases of Madlener ligations from the literature with a failure rate of 0.6 per cent compared with an 0.3 per cent failure rate for the Pomeroy method. He concluded that the Madlener method is unsound both biologically and mechanically. Colmeiro-Laforet[5] in 1950 collected 2,936 cases of Madlener ligations performed in the previous 10 years with a failure rate of 1.56 per cent. Several large series of tubal ligations by the Pomeroy method have been reported with a lower rate of failure. Irving[6] in 1950 reported 814 cases of sterilization by his method with no failures. This is the largest collection of tubal ligations without a failure so far reported and, if confirmed, this method should be adopted.

Since some of the staff have had either a very low incidence of pregnancy or no pregnancies after Madlener tubal ligations, it has seemed that it is not the method but the surgeon who was at fault. We have, therefore, continued with this method, trying to make it perfect, rather than adopting other methods each of which, with the possible exception of Irving's, results in some failures.

Since early 1946 we have followed the original Madlener method. However, during the entire period covered by this paper, we used the broader base portion of the Payr clamp to crush the tube. Recently we have been using the end of the clamp because it crushes more adequately; hence, faulty crushing might in part explain our persistently high failure rate. In the period of time since the last report (July 1, 1945) until July 1, 1951, we have performed 565 tubal ligations, the majority of which were of the Madlener type, with 18 subsequent pregnancies, giving a failure rate of 3.2 per cent. Five hundred thirty-nine of these followed delivery (318 post partum and 221 in conjunction with cesarean section). There have been only 26 gynecological tubal ligations, primarily following therapeutic abortion (abdominal hysterotomy—before 28 weeks of gestation). During the same period we delivered 23,253 patients; thus our incidence of tubal ligation is 2.3 per cent of all patients delivered. The failure rate in postpartum ligations is 3.1 per cent compared with 3.6 per cent in ligations performed with cesarean section. There have been no failures in the gynecologic patients, but the number is small. With the exception of the first year, the failure rate has decreased, as shown in Table I.

TABLE I. TUBAL LIGATIONS AND FAILURES

	POST PARTUM			CESAREAN SECTION			GYNECOLOGICAL		TOTAL		
		FAILED			FAILED			FAILED		FAILED	
YEAR	NO.	NUMBER	%	NO.	NUMBER	%	NO.	%	NO.	NUMBER	%
1945-1946	69	5	7.2	27	3	11.1	1	0	97	8	8.3
1946-1947	45	2	4.4	53	1	1.9	4	0	102	3	2.9
1947-1948	50	2	4.0	46	1	2.2	3	0	99	3	3.0
1948-1949	47	0	0	38	1	2.6	1	0	86	1	1.2
1949-1950	52	1	1.9	30	1	3.3	11	0	93	2	2.2
1950-1951	55	0	0	27	1	3.7	6	0	88	1	1.1
Total	318	10	3.1	221	8	3.6	26	0	565	18	3.2

There were 328 staff patients with a failure rate of 2.8 per cent; 137 university staff private patients with a failure rate of 4.4 per cent; and 100 courtesy staff private patients with a failure rate of 4.0 per cent. If the staff cases in which sodium morrhuate was used were deleted, the staff failure rate would become 3.7 per cent; hence we feel that the difference in failure rates may be at least in part explained by the wider use of sodium morrhuate in staff tubal ligations (Table II).

TABLE II. COMPARISON OF PREGNANCY RATES AFTER TUBAL LIGATION FOR THREE SERVICES

	POST PARTUM		CESAREAN SECTION		GYNECOLOGICAL		TOTAL	
		FAILED		FAILED		FAILED		FAILED
SERVICE	NUMBER	%	NUMBER	%	NUMBER	%	NUMBER	%
Staff	218	2.8	96	2.1	14	0	328	2.8
Private	53	1.9	75	6.7	9	0	137	4.4
Courtesy	47	6.4	50	2.0	3	0	100	4.0
Total	318	(10) 3.1	221	(8) 3.6	26	0	565	(18) 3.2

Studies of the ages and parity of the patients, as well as the time of tubal ligation were made. None of these seemed to be concerned in the failure rate.

Krieg[7] in 1945 reported chemical cauterization of the Fallopian tubes of bitches combined with the Madlener method. Serial sections postoperatively revealed that Carnoy's solution and 75 per cent phenol caused complete destruction in most instances. In his opinion, the reactions from sodium morrhuate were so mild that this agent was considered inadequate.

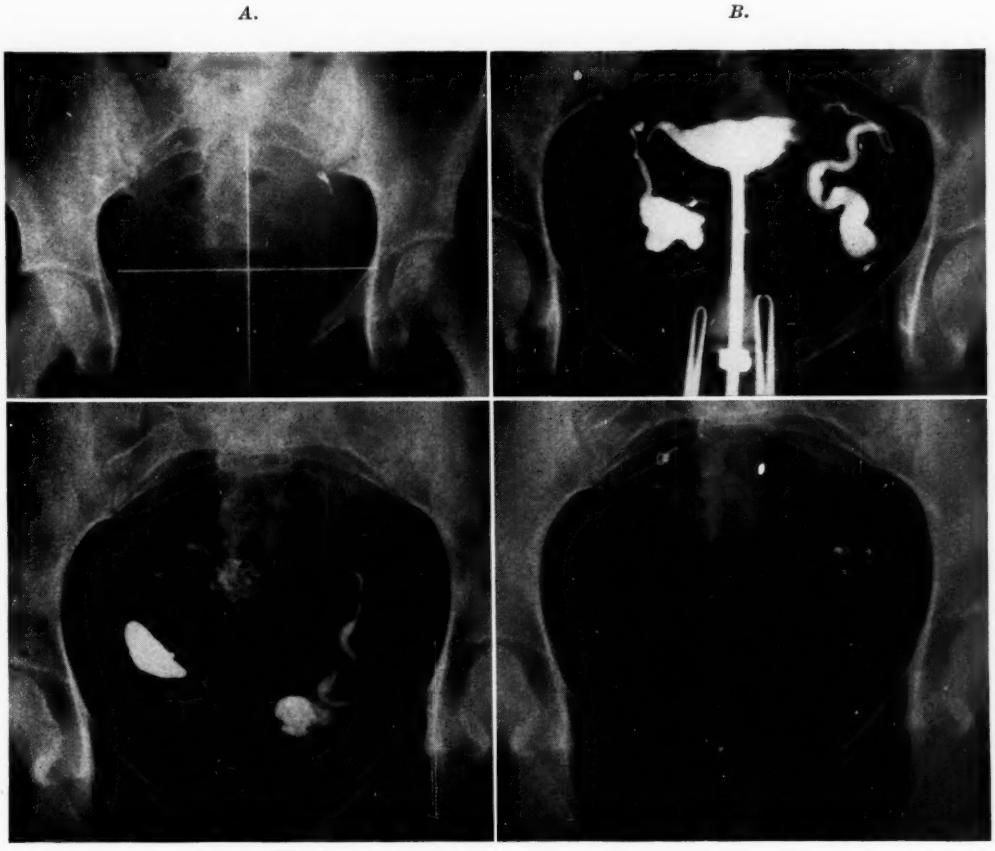

Fig. 1.—*A*, Control x-ray shows tantalum wire in place ten days after delivery. *B*, Lipiodol filled both tubes when injected 15 weeks after delivery. *C*, Film taken twenty-four hours after injection. *D*, Another x-ray film eight weeks later showed complete absence of the previously injected Lipiodol (absorbed or drained through uterus).

We have carried out experiments in rabbits in an attempt to determine the sclerosing effect of sodium morrhuate and other agents on the lining of the tube. In the earlier experiments, sodium morrhuate was injected into the frimbriated end of the rabbit tube. This was followed by a Madlener-type tubal ligation. This method was unsatisfactory because, unlike the results in Krieg's experiments, the ligated loop sloughed off and healing was so complete that it was impossible to get microscopic sections through the site of ligation. In later experiments we injected the morrhuate solution into the

tube as before but this time a segment of the tube was isolated by ligating each end in close proximity to the tube so as not to destroy the blood supply. This method caused a hydrosalpinx with mild inflammatory changes in each instance.

Using Lipiodol and tantalum tape as markers for the x-ray examination, we have been able to study whether or not tubal occlusion is present in women without having to resort to subsequent laparotomies or an attempt to transpose findings in experimental animals to what might happen in human beings.

We injected sodium morrhuate, 95 per cent alcohol, or pure phenol into the wall of the tube at its junction with the uterus with the hope of destroying the lumen. When the tubal ligation was carried out in the routine procedure, tantalum wire was placed at the site of the ligation. About three months later Lipiodol was injected into the uterus.

Fig. 2.—Shows tantalum wire in place but Lipiodol did not enter either tube because lumen had been blocked by the injection of sodium morrhuate into the tubal wall near the uterus.

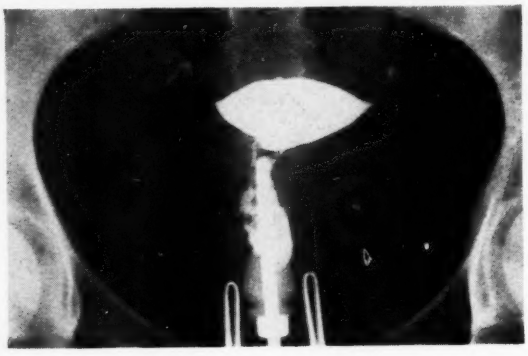

Fig. 3.—Similar blockage of tubal lumen due to injection of 95 per cent alcohol into tubal wall near uterus.

Fig. 1, *A* shows a control film and 1, *B* shows each tube filled. Fig. 1, *C* shows the tubes containing Lipiodol twenty-four hours later. Another x-ray film, Fig. 1, *D*, eight weeks later, shows complete disappearance of the Lipiodol.

Fig. 2 shows a similar Lipiodol test, but sodium morrhuate had been injected into the wall of both tubes, and Lipiodol did not enter either tube. This method of blocking the tubes on further use was not very successful.

Fig. 3 shows that 95 per cent alcohol injected into the tube wall near the uterus prevented the subsequent entrance of Lipiodol. In this case both tubes were blocked, but in other cases this method was not always successful.

Fig. 4 shows filling of the right tube after the usual Madlener type of ligation of both tubes and an interstitial injection of sodium morrhuate into the left tube only, near its junction with the uterus. Lipiodol filled the right tube but not the left tube.

Fig. 5 shows the uterus and left tube of a patient who had had sodium morrhuate injected into the lumen of the right tube. Both tubes were then crushed and ligated with the Madlener method. When Lipiodol was injected some months later, it did not enter the right tube, the mucosa of which had presumably been destroyed by the sclerosive agent.

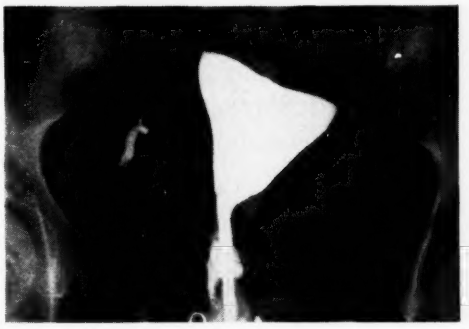

Fig. 4.—Shows filling of right tube but not the left. Sodium morrhuate had been injected into the left tubal wall near the uterus.

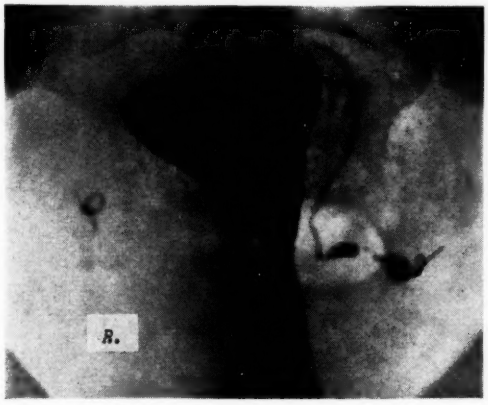

Fig. 5.—Shows tantalum wire in place and filling of left tube but not of right. The sodium morrhuate had been injected into the lumen of the right tube.

Since the latter part of 1947, we have used sodium morrhuate in addition to the original Madlener method in 130 cases with a minimum follow-up of over two years. One cubic centimeter of 5 per cent sodium morrhuate with 2 per cent benzyl alcohol was injected by means of a Eustachian tube cannula into the fimbriated end of each Fallopian tube; immediately following this a Madlener tubal ligation was performed. To date we have had no failures. This compares with a 3.4 per cent failure rate over the same period of time in cases in which the Madlener technique alone was used. Ninety-five per cent alcohol has been used in a few cases, but the number is too small to warrant any conclusions (Table III).

TABLE III. COMPARISON OF TUBAL LIGATION BY THE MADLENER METHOD AND WITH THE ADDITION OF SODIUM MORRHUATE

	MADLENER METHOD ONLY			WITH SODIUM MORRHUATE		
		FAILED			FAILED	
YEAR	NO.	NUMBER	%	NO.	NUMBER	%
1945-1946	97	8	8.3	0	-	-
1946-1947	102	3	2.9	0	-	-
1947-1948	92	3	3.3	7	0	0
1948-1949	65	1	1.5	21	0	0
1949-1950	46	2	4.4	47	0	0
1950-1951	33	1	3.0	55	0	0
Total	435	18	4.1	130	0	0

In the period from July, 1951, to July, 1953, an additional 144 tubal ligations were performed on postpartum patients. Eighty-eight of these were done by the Madlener method with the addition of sodium morrhuate. So far as we know, there have been no failures but the follow-up period is short.

There have been very few serious complications or fatalities after tubal ligation reported in the literature. Nevertheless, it is a major operative procedure and, while we have had no fatalities, we have had one evisceration. There is an inevitable mortality associated with the procedure, and the doctor should therefore be certain of his indication and should use an accepted technique without any modification.

Blockage of the tube has been produced by electrical coagulation. This method cannot be used if explosive anesthetic agents are used; it also requires special apparatus.

Summary

Five hundred sixty-five Madlener-type tubal ligations were performed during a six-year period with pregnancy occurring in 18, or 3.2 per cent.

The incidence of tubal ligation was 2.3 per cent in 23,253 deliveries of infants that weighed 1,000 grams or more.

The failure rate was not affected by the age or the parity of the woman.

Seventy-two per cent of the tubal ligations were performed within the first 24 hours following delivery.

An experimental method is described for determining tubal patency in the woman after "sterilization," by tubal ligation.

Since 1947, over 200 patients have had sodium morruhate injected into each tube and then the Madlener type of ligation performed. In an interval of over two years there have been no failures in this group.

References

1. Dieckmann, Wm. J., and Hauser, E. B.: AM. J. OBST. & GYNEC. **55**: 308, 1948.
2. Madlener, M.: Zentralbl. f. Gynäk. **41**: 331, 1941.
3. Dippel, L. A.: Surg., Gynec. & Obst. **71**: 94, 1940.
4. Knight, R. V.: AM. J. OBST. & GYNEC. **51**: 201, 1946.
5. Colmeiro-Laforet, C.: Rev. españ. obst. y ginec. **9**: 122, 1950.
6. Irving, F. C.: AM. J. OBST. & GYNEC. **60**: 1101, 1950.
7. Krieg, E. G.: Surg., Gynec. & Obst. **81**: 331, 1945.

PREGNANCY AND PULMONARY RESECTION

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SINCE 1901, when Heidenhain[1] performed the first successful lobectomy, and 1931, when Nissen[2] accomplished the first successful pneumonectomy, pulmonary resection has been developed into a major form of therapy for an increasing number of pulmonary diseases. A review of the literature reveals that a great many women with childbearing potentialities have had pulmonary resections. Indeed, six of the first eight successful pneumonectomies involved women either before or during the childbearing years.[2, 3, 4, 5, 6]

Since the indications for pulmonary resection are being expanded, it is obvious that surgeons and obstetricians are going to be increasingly concerned with the ability of patients with diminished pulmonary tissue to meet the demands of pregnancy. Even more important will be the question of whether pulmonary resection can be performed during pregnancy with safety to the mother and fetus. It seems worth while, therefore, to collect from the literature the reports of pregnancy intimately associated with pulmonary resection and to record the experience of the Johns Hopkins Hospital with this combination.

Review of the Literature

We have found specific reference to forty-two cases in which pregnancy has followed or has been associated with resection of major anatomical divisions of the lung. A number of these are known only because of a casual remark in the follow-up report that the patient has had a pregnancy since operation. There are some additional reports of cases of major thoracic surgery followed by pregnancy in which it is uncertain what type of procedure was done. Undoubtedly there are more unreported cases, since it is only in the past few years that surgeons and obstetricians have become concerned enough with the childbearing careers of such women to report their progress through pregnancy in any detail.

Pregnancy and Lobectomy.—Tyson,[7] discussing lobectomy for pulmonary cysts, reported on a patient who since lobectomy in 1937 has "been married, and has been delivered of a healthy baby without ill effects." Bryce and Mills[8] reported three cases following lobectomy for bronchiectasis. One had a therapeutic abortion at twelve weeks for extensive bronchiectasis and bronchopleural fistula. Two had uneventful pregnancies, one delivering a 5½ pound infant that died at 15 days, and the other delivering at term. Souders,[9] reviewing the management of 277 cases of bronchiectasis, reported that several amenorrheic or infertile women had resumed their menses or become pregnant after lobectomy. Ellman[10] stated that successful pregnancy has occurred following lobectomy

and cited a case (apparently the second case reported by Bryce and Mills). Schaeffer[11] remarked that he had followed six uneventful pregnancies after lobectomy or pulmonary resections. Folsome and Kuntze,[12] reviewing a series of pregnancies following major thoracic surgery for tuberculosis, reported on two patients who had uneventful pregnancies and deliveries after previous lobectomy.

There are three reports of lobectomy during pregnancy. Sonzini Astudillo[13] reported left lower lobe lobectomy at sixteen weeks for suppurative echinococcus cyst. Unfortunately, no details of the subsequent course are available, except that abortion did not occur in the immediate postoperative period. Guzman and co-authors[14] reported a right upper lobe lobectomy for tuberculosis at eighteen weeks with subsequent full-term delivery after an uneventful pregnancy. Schaeffer and Epstein[15] reported an exactly similar case done at what was later found to be the eighth week of pregnancy. Delivery after an uneventful prenatal course was accomplished by low forceps under caudal analgesia.

Pregnancy and Pneumonectomy.—In 1942, Hepburn and Dauphinee,[16] reporting a pneumonectomy for hemangioma of the lung, casually mentioned that then, two years after surgery, the patient was six months pregnant. Wodehouse[17] in 1948 stated that this same patient had now had two children. Nissen,[18] in recording the history of pneumonectomy, reported that Haight's[5] first case had one child and was in excellent general health.

Long, Wester, Willson, and Rosemond[19] reported in great detail the pregnancy of a 40-year-old primigravida three years after right pneumonectomy for adenocarcinoma. She showed an extremely low respiratory reserve (vital capacity only 50 per cent of normal) which remained relatively constant during pregnancy. Her venous pressure, on the other hand, rose from 60 mm. of saline early in pregnancy to 160 at 34 weeks and then fell to 100 mm. of saline only to rise to 208 at term. She had increased exertional dyspnea and recurrent episodes of chest pain as pregnancy advanced. Labor lasted only six hours, however, and was terminated by low forceps under saddle block anesthesia with delivery of a 3,629 gram infant.

Ellman[10] reported upon a patient who aborted five years after pneumonectomy for bronchiectasis and who was six months pregnant and healthy six years after the pulmonary surgery. Schaeffer,[11] as previously mentioned, has followed six patients through uneventful pregnancies following lobectomy or pulmonary resection for tuberculosis.

Folsome and Kuntze[12] reported twenty pregnancies in twelve patients who had pneumonectomies for tuberculosis. There were two spontaneous abortions, four therapeutic abortions, three premature births, and eleven term births in this series. Five of the deliveries were spontaneous, five were forceps deliveries, three were cesarean sections, and one a cesarean hysterectomy for rupture of a previous section scar. All of the labors were terminated within twenty-four hours. The authors stated that "dyspnea during pregnancy or labor was not a factor in any of our cases." Greeley, discussing Folsome and Kuntze's paper at the New York Obstetrical Society in December, 1952, reported upon a

patient who had active tuberculosis in the remaining lung, whose pregnancy was marked by tachycardia, orthopnea, and very low vital capacity, but whose labor and delivery were uneventful. Pisani in the same discussion reported that during 1952 Veterans Administration hospitals had successful outcomes with twelve cases of pregnancy following major thoracic surgery.

Gaensler and co-workers[22] reported that they have followed eight women through uneventful pregnancy and delivery after pneumonectomy. They reported pulmonary function studies on two patients who had had both pneumonectomy and thoracoplasty. Neither patient had dyspnea during pregnancy or showed as much reduction in respiratory reserve as the patient of Long and co-workers[19] previously mentioned. One of Gaensler's patients, indeed, had a right thoracoplasty and left pneumonectomy before pregnancy. Another case in which uneventful pregnancy followed pneumonectomy for tuberculosis has been reported to us.[23]

Thompson and Bressler[24] reported a pneumonectomy for unilateral tuberculosis in the twenty-fourth week of pregnancy. Except for tachycardia, the prenatal course was uneventful. Labor occurred in the thirty-fifth week and delivery of a 2,300 gram infant was accomplished by low forceps after eight and one-half hours of labor. Draa and Baum[25] state that "thoracoplasty, phrenic nerve crush, and lung resection have been done to treat tuberculosis . . . in pregnant patients." Folsome and Kuntze[12] mention Thompson and Bressler's case and record another case of pneumonectomy during pregnancy, this time with full-term spontaneous delivery.

Material

A review of the case records of the Johns Hopkins Hospital revealed fifteen cases in which pregnancy was intimately related to pulmonary resection. These cases extend over a period of twenty years from 1933 (Rienhoff's[4] second pneumonectomy case) to 1953. There are two cases in which lobectomy was performed just prior to pregnancy, six cases of lobectomy during pregnancy, three cases of pregnancy following resection of two lobes, and four cases of pregnancy following pneumonectomy. The salient features of these cases are given in Tables I-IV. Since details of most of the cases in the literature are not given, it seems worth while to present our series as case reports.

Case Reports

I. Pregnancy Immediately Following Pneumonectomy (Table I).—

CASE 1.—D. T., a 28-year-old white para 2-0-1-2, had a left lower lobe lobectomy performed on May 24, 1946, for bronchiectasis. Her last menstrual period was June 2, 1946. In September, 1946, the sixteenth week of pregnancy, a therapeutic abortion by curettage was carried out on the Gynecological Service. This procedure was advised by the medical consultant in the belief that there had been no time prior to pregnancy for compensatory changes to take place in the lung. This patient had no subsequent pregnancies. In May, 1952, a modified Wertheim hysterectomy was performed for intraepithelial carcinoma of the cervix.

CASE 2.—M. B., a 17-year-old white para 1-0-0-1, with an intra-auricular septal defect, was subjected to left lower lobe lobectomy for bronchiectasis on June 30, 1949. Her last recorded menstrual period was June 17, 1949. Her subsequent childbearing career, however,

TABLE I. PREGNANCY IMMEDIATELY FOLLOWING PULMONARY RESECTION

PATIENT	RACE	AGE	PARITY	YEAR	EXTENT OF SURGERY	LESION	PREGNANCY	COMPLICATIONS	OUTCOME, MOTHER, CHILD
Case 1, D. T., No. 381995	White	28	2-0-1-2	1946	Left lower lobe	Bronchiectasis	8 weeks after	Cough	Therapeutic abortion at 12 weeks
Case 2, M. B., No. 497444	White	17	1-0-0-1	1949	Left lower lobe	Bronchiectasis	4 weeks after	Intra-auricular septal defect	Delivered at 35 weeks 2,353 gram infant, living

TABLE II. PULMONARY RESECTION DURING PREGNANCY

PATIENT	RACE	AGE	PARITY	YEAR	EXTENT OF SURGERY	LESION	PREGNANCY	COMPLICATIONS	OUTCOME, MOTHER, CHILD
Case 3, A. H., No. 154208	Negro	22	1-0-0-1	1939	Left lower lobe	Bronchiectasis	17 weeks	Empyema, pneumonia	Aborted 2 weeks later Died 3 weeks later
Case 4, E. F., No. 323259	White	20	1-0-0-1	1948	Left lower lobe	Bronchiectasis	13 weeks	Empyema, bronchopleural fistula	Therapeutic abortion 1 week prior to lobectomy
Case 5, M. T., No. 453938	White	22	3-0-0-2	1948	Left lower lobe	Bronchiectasis	20 weeks	Pleural effusion	Delivered elsewhere at term, living
Case 6, B. W., No. 339363	White	28	1-0-0-1	1948	Right lower lobe	Bronchiectasis	9 weeks	Cough	Delivered at term 3,050 gram infant, living
Case 7, E. M., No. 368775	White	32	4-0-2-4	1952	Left lower lobe	Bronchial adenoma	12 weeks	None	Delivered at term 3,575 gram infant, living
Case 8, K. B., No. 636037	White	26	2-0-0-2	1953	Right upper lobe	Tuberculosis	17 weeks	None	Delivered elsewhere at term, living

suggests that pregnancy began after operation. Her prenatal course was uneventful. Delivery by low forceps of a 2,353 gram male infant under saddle block anesthesia was effected on March 15, 1950, after five hours of labor. She has subsequently delivered two 2,300 gram infants in the thirty-sixth week of pregnancy (1952, 1953). It appears, therefore, most likely that the 1949-1950 pregnancy began after pneumonectomy and was of thirty-six weeks' duration rather than thirty-nine weeks.

II. Lobectomy During Pregnancy (Table II).—

CASE 3.—A. H., a 22-year-old Negro para 1-0-0-1, had a left lower lobe lobectomy for bronchiectasis on April 15, 1939. The patient was known to be sixteen weeks pregnant at the time of operation, but pregnancy was thought to be no contraindication to pulmonary surgery. On the fifth postoperative day she developed empyema with a temperature of 101 to 106° F. This was treated with sulfapyridine, but the fever continued. She aborted without difficulty on the fourteenth day. The fever continued and she gradually became more ill. Death occurred on the twenty-second postoperative day. Autopsy showed a clean uterus, bronchopleural fistula, empyema, multiple abscesses of the left lung, and bilateral lobular pneumonia.

CASE 4.—E. F., a 20-year-old white para 1-0-0-1, was found to be eleven weeks pregnant when admitted in March, 1949, for pulmonary surgery because of bronchiectasis. In the hospital she was found to have extensive bronchiectasis involving the upper and lower lobes of the left lung and the lower lobe of the right lung. The obstetrical consultant advised therapeutic abortion only if more than two lobes were removed on the basis that the remaining lung tissue would be inadequate to support the pregnancy. The surgical and medical opinion, however, favored therapeutic abortion prior to any lung surgery. Accordingly, therapeutic abortion by curettage was carried out under spinal anesthesia on March 22, 1948. Left lower lobe lobectomy was then performed on March 30, 1948. In 1949 the patient had a successful pregnancy with delivery in another hospital.

CASE 5.—M. T., a 22-pear-old white para 3-0-0-2, had a left lower lobe lobectomy for bronchiectasis in the twentieth week of pregnancy on March 31, 1948. She required repeated postoperative thoracenteses but otherwise did well. She left the hospital against advice on the thirteenth day. We have not seen her since, but she is known to have delivered uneventfully at term.

CASE 6.—B. W., a 28-year-old white para 1-0-0-1, had a right lower lobe lobectomy for bronchiectasis on Nov. 11, 1947, in what was subsequently found to be the ninth week of pregnancy. Her pregnancy was complicated only by a productive cough due to right middle lobe bronchiectasis. She was delivered spontaneously in June, 1948, at term after a five-hour labor under caudal analgesia of a 3,050 gram female infant. She had another uneventful pregnancy elsewhere in 1950, and in February, 1951, a right middle lobe lobectomy was performed. We have not heard from her since 1951.

CASE 7.—E. M., a 32-year-old white para 4-0-2-4, was found to have a bronchial adenoma in the left lower main stem bronchus when fourteen weeks pregnant. On the advice of the obstetrical consultant, to treat the tumor without regard to the pregnancy, a left lower lobe lobectomy was carried out on March 6, 1952. The pregnancy progressed uneventfully to term. After a five-hour labor under barbiturate sedation she delivered spontaneously on Sept. 5, 1952, under nitrous oxide-oxygen anesthesia, a 3,575 gram female infant.

CASE 8.—K. B., a 26-year-old white para 2-0-0-2, was found to have active pulmonary tuberculosis confined to the right upper lobe when seven weeks pregnant. Lobectomy was advised, but, on the recommendation of the obstetrical consultant, was postponed until after the sixteenth week of pregnancy. Right upper lobe lobectomy was performed on April 11, 1953, in the seventeenth week of pregnancy. Five days after operation she had a transient episode of vaginal spotting. Her pregnancy otherwise was uneventful. She delivered elsewhere at term without event.

TABLE III. PREGNANCY FOLLOWING EXTENSIVE PULMONARY RESECTION

PATIENT	RACE	AGE	PARITY	YEAR	EXTENT OF SURGERY	LESION	PREGNANCY	COMPLICATIONS	OUTCOME, MOTHER, CHILD
Case 9, C. H., No. 280329	White	29	0-0-0-0	1948	Right lower, middle lobe, 1943	Bronchiectasis	4 years after	Rh sensitization. Cough, dyspnea	Delivered at term, stillbirth
Case 10, L. A., No. 258044	White	22	0-0-0-0	1948	Right lower, middle lobe, 1942	Bronchiectasis	6 years after	Cough	Delivered at 34 weeks, 2,975 gram infant, living
Case 11, V. C., No. 560649	White	25	0-0-0-0	1951	Right lower, middle lobe, 1944	Bronchiectasis	7 years after	None	Delivered at term 2,900 gram infant, living
				1953			9 years after	None	Delivered at term 3,660 gram infant, living

TABLE IV. PREGNANCY FOLLOWING PNEUMONECTOMY

PATIENT	RACE	AGE	PARITY	YEAR	EXTENT OF SURGERY	LESION	PREGNANCY	COMPLICATIONS	OUTCOME, MOTHER, CHILD
Case 12, H. M., No. 119888	White	27	0-0-0-0	1937	Left lung, 1933	? Bronchial adenoma	5 years after	Postdelivery pneumonia	Cesarean section at 38 weeks; 3,400 gram infant, living
Case 15, E. N., No. 570150	Negro	34	1-0-0-1	1951	Right lung, thoracoplasty, 1948	Tuberculosis	3 years after	None	Delivered at 33 weeks, 2,300 gram infant, living
Case 13, L. A., No. 258044	White	25	1-0-0-1	1952	Two-stage right lung, 1949	Bronchiectasis	3 years after	Cyanosis at 38 weeks	Delivered at 39 weeks, 3,225 gram infant, living
Case 14, A. P., No. 551257	Negro	24	0-0-0-0	1951	Right lung, thoracoplasty, 1950	Tuberculosis	1 year after	Dyspnea at 38 weeks; cyanosis at 38 weeks	Delivered at term, 2,910 gram infant, living
				1953			3 years after	None	Delivered at 38 weeks, 3,185 gram infant, living

III. Pregnancy Following Extensive Pulmonary Resection (Table III).—

CASE 9.—C. H., a 29-year-old white primigravida, was first seen by the obstetrician in February, 1948, in the fifteenth week of pregnancy. She had had a right middle and lower lobe lobectomy for bronchiectasis in 1944. One blood transfusion had been given during the operation. There was residual bronchiectasis in the right upper and left lower lobes. She was discovered to be Rh negative with antibodies present and to have an Rh-positive homozygous husband. Her prenatal course was marked by moderate dyspnea and cough. The fetal heartbeat disappeared three days before delivery. She delivered a completely macerated erythroblastotic 2,450 gram male infant on Aug. 16, 1948, under saddle block anesthesia after ten hours of labor. Her postpartum course was uneventful. The patient refused contraceptive advice on religious grounds and has not been seen since.

CASE 10.—L. A., a 22-year-old white primigravida, was first seen by the obstetrician in August, 1948, in the twenty-fifth week of pregnancy. In June, 1942, a right middle and lower lobe lobectomy had been performed for bronchietasis. Her prenatal course was marked by chronic cough suggestive of residual right upper lobe bronchiectasis. Delivery of a 2,975 gram female infant was accomplished six weeks before term by low forceps after five hours of labor. Her postpartum course was uneventful. Her subsequent history is related in the report of Case 13.

CASE 11.—V. C., a 25-year-old white primigravida, was first seen by the obstetrician in January, 1951, in the seventeenth week of pregnancy. In 1944, she had had a right middle and lower lobe lobectomy for bronchiectasis. Her prenatal course was entirely uneventful. From the twenty-fifth week of pregnancy she was studied at two-week intervals by vital capacity, venous pressure, and arterial oxygen saturation determinations. These studies were repeated during labor, five days post partum, and six weeks post partum. Her vital capacity was constant at 3,000 c.c., or 91 per cent of normal, and the venous pressure varied from 60 to 115 mm. of saline. Her arterial oxygen saturation was consistently about 94.5 per cent. Labor at term on June 12, 1951, lasted six hours under caudal analgesia, and was terminated by low forceps delivery of a 2,900 gram female infant. Her postpartum course was uneventful.

Her second pregnancy occurred in 1952 and was again uneventful. Labor began at term on Jan. 3, 1953. After four hours under Nembutal and scopolamine analgesia she was delivered spontaneously with nitrous oxide-oxygen anesthesia of a 3,660 gram female infant. Her postpartum course was again uneventful.

IV. Pregnancy Following Pneumonectomy (Table IV).—

CASE 12.—H. M., a 27-year-old white primigravida, was first seen by the obstetrician in March, 1937, in the tenth week of pregnancy. This patient had been Dr. Rienhoff's[4] second pneumonectomy case. On Nov. 3, 1933, a left pneumonectomy was performed for bronchial carcinoma. This tumor, in all probability, was actually a bronchial adenoma. Her vital capacity after operation was 2,100 c.c., or 67.5 per cent of normal.

Since at the time of her pregnancy (1937) little was known concerning her prognosis and nothing was known of the effects of pneumonectomy on pregnancy, she was offered a choice of immediate termination of pregnancy, or cesarean section at term (to spare her the muscular strain of labor) and tubal sterilization. She chose the latter. She had had one-pillow orthopnea since operation, but had been otherwise well. The orthopnea increased during pregnancy so that she needed two pillows to be comfortable lying down. Otherwise her pregnancy was uneventful. At term her vital capacity was 2,270 c.c., or 73 per cent of normal, representing an increase over her prepregnancy vital capacity of 5.5 per cent.

Classical cesarean section and Madlener tubal sterilization were carried out on Oct. 13, 1937, and a 3,400 gram male infant was obtained. An attempt at spinal anesthesia with procaine failed and the procedure was carried out under nitrous oxide-oxygen-ether anesthesia. Her postoperative course was stormy with temperatures ranging from 100° to 106° F. for

eleven days due to bronchopneumonia of the right middle and upper lobes. This was due to Vincent's organism and responded to sulfanilamide and neoarsphenamine. The patient was afebrile for eighteen days prior to discharge on the twenty-eighth postoperative day.

The patient has remained healthy. She has had no further pregnancies. She was last seen in the hospital in March, 1951, when a curettage for menometrorrhagia was performed.

CASE 13. L. A., a 25-year-old white para 1-0-0-1 (whose previous history is related in Case 10) was seen again by the obstetrician in January, 1952, in the eighth week of pregnancy. After her previous delivery, because of increasing productive cough and bronchiectasis of the right upper lobe, she had the remaining right upper lobe removed. This procedure was performed with great difficulty in January, 1949.

Her prenatal course was uneventful. There were no symptoms of respiratory difficulty. Her vital capacity ranged from 1,700 to 2,200 c.c. (56 to 73 per cent of normal). In midpregnancy, from seventeen to thirty weeks, her vital capacity remained 1,800 c.c. (60 per cent of normal). From thirty-four weeks to thirty-eight weeks it rose to 2,100 to 2,200 c.c. (69 to 73 per cent of normal), but two days before delivery it was only 1,400 c.c. (46 per cent of normal). At this time there was a transient episode of minimal cyanosis associated with edema. Her venous pressure remained at low normal levels throughout (41 to 107 mm. of saline). Certain pulmonary function studies carried out before and after pregnancy by the Respiratory Physiology Laboratory are recorded in Table V.

TABLE V. PULMONARY FUNCTION STUDIES IN PREGNANCY FOLLOWING PNEUMONECTOMY (CASE 13, L. A.)

DETERMINATION	PREDICTED	13 WEEKS	34 WEEKS	6 WEEKS POST PARTUM
Vital capacity, c.c.	3,020	2,260	2,100	2,020
Expiratory reserve volume, c.c.	800	1,060		
Residual volume, c.c.	760	1,200		
Total lung capacity, c.c.	3,780	3,460		
Residual volume as per cent of total lung capacity	20	35		
Maximum breathing capacity, liters per minute	91	88	70	78
Ventilation, liters per minute	3,900-7,000	8,200		
Tidal volume, c.c. per minute		318		
Dead space ventilation, per cent	<30	40		25
Diffusing capacity, ml. O_2 per mm. Hg	35			23
Venous admixture ratio, per cent	<6	<1		6

The lung volumes are as expected with loss of lung tissue. Removal of one lung has reduced the maximal diffusing capacity to about two-thirds of normal rather than one-half of normal.

Labor occurred on Aug. 3, 1952, in the thirty-eighth week of pregnancy and lasted five hours without analgesia. Delivery of a 3,220 gram male infant was effected by low forceps under pudendal block and nitrous oxide-oxygen anesthesia. Her postpartum course was uneventful.

CASE 14.—A. P., a 24-year-old Negro primipara, was admitted to the hospital in September, 1950, in the fifteenth week of pregnancy for evaluation because of a previous pneumonectomy and eight-rib thoracoplasty. This procedure had been done in another hospital in July, 1949, because of extensive unilateral tuberculosis and inability to accomplish pneumothorax. Following operation she had remained well, though she was easily fatigued. Her last menstrual period occurred in June, 1950, about eleven months after operation.

In the hospital no evidence of tuberculosis in the left lung could be found. Her vital capacity after several tests ranged from 1,000 to 1,200 c.c. (33 to 46 per cent of normal).

Her venous pressure was 70 mm. of saline. Medical consultants advised interruption of pregnancy on the basis of restricted respiratory reserve for pregnancy and the danger of reactivating the so recently eradicated tuberculosis. The patient, however, refused interruption of pregnancy, and in her desire for a child accepted hospitalization until delivery. During the ensuing twenty-five weeks she remained well. Leaves of absence were granted on holidays and occupational therapy was provided. Her vital capacity checked at weekly intervals rose to 1,700 c.c., or 57 per cent of normal, by the twenty-first week where it remained until the thirty-second week. During the last eight weeks her vital capacity was 1,000 c.c. or 33 per cent of normal. From time to time in the last trimester there were subjective episodes of dyspnea (her respiratory rate never exceeded 28 per minute) traceable in most instances to psychosomatic problems arising from the prolonged hospitalization. In the thirty-eighth week there was a 48 hour episode of mild cyanosis confirmed by an arterial oxygen saturation of 88 per cent. Her venous pressure remained constant at 70 mm. of saline.

Labor occurred at term in March, 1951, and was conducted under continuous caudal analgesia. Delivery of a 2,910 gram male infant was effected by low forceps after four and one-half hours of labor. Her postpartum course was uneventful for fourteen days in the hospital. Her vital capacity continued to range from 1,000 to 1,200 c.c. (33 to 46 per cent of normal) and her venous pressure remained unchanged. Similar findings were obtained at six weeks post partum when she was given contraceptive advice.

In spite of the use of the diaphragm, she became pregnant in 1952 and was first seen in October in the nineteenth week of pregnancy. She was immediately hospitalized for evaluation. Her vital capacity ranged from 1,100 to 1,300 c.c. (38 to 46 per cent of normal). Studies carried out by the Respiratory Physiology Laboratory are recorded in Table VI.

TABLE VI. PULMONARY FUNCTION STUDIES IN PREGNANCY FOLLOWING PNEUMONECTOMY WITH THORACOPLASTY (CASE 14, A. P.)

DETERMINATION	PREDICTED	21 WEEKS	28 WEEKS
Vital capacity, c.c.	2,890	1,298	1,263
Maximum breathing capacity, liters per minute	86	27	33
Ventilation, liters per minute	3,200	8,380	
Dead space ventilation, per cent	<30	25	
Venous admixture ratio, per cent	<6	6	

There is hyperventilation with normal ventilation-perfusion relationships. The vital capacity is about normal for one lung, but the maximum breathing capacity is reduced far below normal for pneumonectomy. However, she it not dyspneic on one flight of stairs.

In view of the good course before, the patient was followed at weekly intervals without hospitalization. Her vital capacity ranged from 1,300 to 1,700 c.c. (48 to 57 per cent of normal), and there was no dyspnea at any time. It was obvious that her ability to lead a relatively normal life avoided the psychosomatic problems which led to subjective dyspnea during the previous enforced hospital stay.

Labor began on Jan. 15, 1953, approximately seven weeks before her calculated date of confinement. After two hours, delivery of a 3,185 gram male infant was effected by low forceps using pudendal block for anesthesia. Her postpartum course was uneventful. Unfortunately, the patient has not returned for further respiratory studies, but she is alive and well.

CASE 15.—E. N., a 34-year-old Negro, para 1-0-0-1, was first seen by the obstetrician in April, 1951, in the twenty-seventh week of pregnancy. The patient had had a previous uncomplicated delivery in 1942. During 1947-1949 she was hospitalized elsewhere for treatment of unilateral pulmonary tuberculosis. Following phrenic nerve crush and pneumoperitoneum there was some improvement. Therefore, in April, 1948, a right pneumonectomy was performed. This was followed by an intractable empyema for which in February and March, 1949, a two-stage eight-rib thoracoplasty was performed. Following discharge from the hospital she remained well and asymptomatic.

Her pregnancy was uneventful. Her vital capacity was reduced to 800 to 900 c.c. (30 to 31 per cent of normal) and fell in the thirty-third week of pregnancy to 700 c.c., or 28 per cent of normal. There was no dyspnea at any time. Her arterial oxygen saturation varied from 92 to 95.5 per cent. Her venous pressure, however, was consistently somewhat elevated to 126.5 to 133 mm. of saline. Labor occurred in the thirty-third week of pregnancy, June 5, 1951. After one hour and forty-five minutes she delivered spontaneously under nitrous oxide-oxygen anesthesia a 2,300 gram male infant. Her vital capacity immediately after delivery was 600 c.c., or 25 per cent of normal, and her arterial oxygen saturation was 95.5 per cent. These values remained constant through her course for six weeks post partum. The venous pressure, however, fell from 126.5 mm. of saline immediately post partum to 100 mm. of saline on the third postpartum day. At six weeks post partum her venous pressure was again elevated to 124 mm. of saline.

The patient developed heart failure nine months post partum and died ten months after delivery. Autopsy showed the following significant items: Cor pulmonale, disseminated tuberculosis of the left lung, and chronic organized right empyema with fistula to the healed thoracoplasty scar.

Comment

There are now fifty-seven known cases of pulmonary resection intimately associated with pregnancy. These fifty-seven patients have had sixty-nine pregnancies: seven terminated by therapeutic abortion, four by spontaneous abortion, eight by premature delivery, and forty-eight by term delivery. The outcome of two cases is unknown. There were fifty-one vaginal deliveries and five cesarean sections. There was one maternal death during the puerperal period due to pulmonary infections. Five infants were lost, one during the neonatal period, and four were stillborn. In only six cases, two from the literature and four from our series, has there been dyspnea or other clinical evidence of respiratory stress due to pregnancy.

It is obvious from a recital of these statistics that these patients not only have an excellent obstetrical record, but also that they have been remarkably free of subjective evidences of undue respiratory strain. In order to pass final judgment, however, on the safety of pregnancy associated with pulmonary resection, an evaluation of respiratory function of such cases during gestation is needed.

Unfortunately such data are scarce. There are none at all relating to one-lobe lobectomy during or followed by pregnancy. It is obvious, however, that single lobectomy does not produce a significant reduction of respiratory tissue. One expects little or no diminution in pulmonary function in such patients provided the remaining lung tissue is relatively normal, and, therefore, one would not expect their pulmonary function in pregnancy to show much deviation from the normal. Our one study of vital capacity following two-lobe lobectomy is in keeping with this expectation, for the vital capacity was consistently about 90 per cent of normal during pregnancy.

There are a few studies of patients with moderate to marked pulmonary insufficiency. Our patient (Case 13) who had had a pneumonectomy showed only one deviation during pregnancy from her normal nonpregnancy function; namely, transient cyanosis and a fall in vital capacity (800 c.c.) just before delivery. The patient reported by Long and co-workers[19] must have had

damage to the remaining lung as evidenced by a vital capacity and maximum breathing capacity about half that of our patient, yet her pulmonary function showed no significant change during pregnancy. Long's patient also showed abnormal venous pressure changes and abnormal overload test response suggesting vascular damage as a result of surgery. Our two patients (Cases 14 and 15) with pneumonectomy and thoracoplasty prior to pregnancy, both of whom had considerable reductions in vital capacity, did not show marked alterations in pulmonary function as pregnancy advanced. Case 14 did experience dyspnea, reduction in vital capacity, and transient cyanosis in one pregnancy, but in a second pregnancy, when freed of psychosomatic stress and allowed more activity, showed no such changes. Case 15 had a vital capacity about one-half to three-fourths that of Case 14, yet had no signs of respiratory stress. On the other hand, she had an elevated venous pressure. Those findings suggested marked damage to the remaining lung which was confirmed at autopsy following her death from heart failure ten months post partum.

Gaensler, whose observations constitute part of a study of pulmonary function in pregnancy,[22, 26, 27] has studied two patients, one with pneumonectomy and space-filling thoracoplasty, and one with left pneumonectomy and right thoracoplasty. Even these patients with marked pulmonary insufficiency showed little or no change in pulmonary function late in pregnancy. As a result of studies made in normal pregnancy by this group of workers certain conclusions regarding the differences in pulmonary function during normal pregnancy and pregnancy complicated by pulmonary insufficiency are possible. Our studies and those of Long and co-workers, though less extensive, support these conclusions in general.

In patients with pulmonary insufficiency due to loss of lung tissue and diminished intrathoracic space, the ventilatory capacity is reduced due to the irreparable loss of vitay capacity. Compensation for this loss is effected by more rapid and more regular breathing and by the decreased resistance of the respiratory passages to the smaller vital capacity (demonstrated by Gaensler by air velocity indices greater than normal). This fact probably accounts for the observation that subjective dyspnea is more common in normal pregnant patients than in those with pulmonary insufficiency. It also accounts for the fact that maximum breathing capacity is not as severely impaired as might be expected.

In pregnancy, hyperventilation generally decreases as pulmonary insufficiency increases. Gaensler's most severely disabled patients showed no true hyperventilation, since their ventilation increased no more than their oxygen uptake. One of our two patients with pneumonectomy and thoracoplasty did, however, show marked hyperventilation. This patient had more extensive collapse of the chest wall than any of Gaensler's patients. The loss of thoracic-cage elasticity and the patient's ready response to psychosomatic factors probably account for this difference.

In normal pregnancy the increased ventilatory requirement is met by increase in depth of respiration. When the total lung volume is markedly

decreased, the elastic limits of the thorax and lungs do not permit such a mechanism to be effective. The pregnant patient with severe pulmonary insufficiency, especially if the thoracic cage is also reduced in size, can, therefore, only handle the increased ventilatory requirement by increasing her respiratory rate.

In both normal pregnancy and pregnancy complicated by pulmonary insufficiency there are no essential changes in vital capacity and maximum breathing capacity as pregnancy advances. In Gaensler's patients the subdivisions of total lung capacity showed the changes characteristic of pregnancy, i.e., breathing with more deflated lungs.

The excellent obstetrical record of the fifty-seven patients who have had pregnancies complicated by pulmonary resection demonstrates that patients with purely restrictive pulmonary insufficiency tolerate pregnancy well. The clinician may accept with security Gaensler's statement that "patients with restrictive ventilatory insufficiency, who are not dyspneic at rest or during slightest exertion, should tolerate pregnancy without difficulty."

Summary

Forty-two cases of pregnancy intimately associated with pulmonary resection have been found in the literature. Fifteen such cases in the records of the Johns Hopkins Hospital have been reviewed. There are now fifty-seven such patients who have had a total of sixty-nine pregnancies. Physiological data on three cases of pregnancy complicated by previous pneumonectomy in the literature and three studied at the Johns Hopkins Hospital are reported.

The following conclusions of clinical significance are drawn from the study of these cases:

1. Pneumonectomy and pulmonary resection are no contraindication to pregnancy provided the patient is not dyspneic at rest or on slight exertion.
2. Patients with pulmonary resections who are not dyspneic under normal conditions go through labor and vaginal delivery without difficulty.
3. Pneumonectomy and lobectomy may be performed during pregnancy with safety to mother and infant, if absolutely essential to the welfare of the mother.
4. Because of their reduced respiratory reserve, pregnant patients with pneumonectomy must be protected from any illness which will tend to reduce this limited reserve.

References

1. Heidenhain, L.: Verhandl. d. deutsch. Gesellsch. f. Chir. 30: 636, 1901.
2. Nissen, R.: Zentralbl. f. Chir. 58: 3003, 1931.
3. Windsberg, E.: Rhode Island M. J. 17: 163, 1934.
4. Rienhoff, W. F., Jr.: Bull. Johns Hopkins Hosp. 53: 390, 1938.
5. Haight, C.: Surg., Gynec. & Obst. 58: 768, 1934.
6. Overholt, R. H.: J. Thoracic Surg. 4: 196, 1934.
7. Tyson, M. D.: Ann. Surg. 118: 50, 1943.
8. Bryce, A. G., and Mills, E. M.: Lancet 247: 786, 1944.
9. Souders, C. R.: Dis. of Chest 16: 381, 1949.
10. Ellman, P.: In Clayton, S., and Oram, S.: Medical Disorders During Pregnancy, New York, 1951, Grune and Stratton.

11. Schaeffer, G.: Obst. & Gynec. Surv. **6**: 767, 1951.
12. Folsome, C. E., and Kuntze, C. D.: AM. J. OBST. & GYNEC. **65**: 1319, 1953.
13. Sonzini Astudillo, C. P.: Rev. clín. españ. **38**: 308, 1950.
14. Guzman, F. L., Jennings, F. L., Popplewell, A. G., and others: Philippine M. A. J. **28**: 214, 1952.
15. Schaeffer, G., and Epstein, H. H.: AM. J. OBST. & GYNEC. **64**: 188, 1952.
16. Hepburn, J., and Dauphinee, J. A.: Am. J. M. Sc. **204**: 681, 1942.
17. Wodehouse, G. E.: J. Thoracic Surg. **17**: 408, 1948.
18. Nissen, R.: Am. J. Surg. **78**: 816, 1949.
19. Long, J. H., Wester, M. R., Willson, J. R., and Rosemond, G. P.: J. A. M. A. **143**: 358, 1950.
20. Greeley, A. V.: Discussion of Folsome, C. E., and Kuntze, C. D.: AM. J. OBST. & GYNEC. **65**: 1319, 1953.
21. Pisani, B. J.: Discussion of Folsome, C. E., and Kuntze, C. D.: AM. J. OBST. & GYNEC. **65**: 1319, 1953.
22. Gaensler, E. A., Patton, W. E., Verstaeten, J. M., and Badger, T. L.: Am. Rev. Tuberc. **67**: 779, 1953.
23. Sadler, W. P.: Personal communication.
24. Thompson, S. A., and Bressler, S.: Surgery **26**: 242, 1949.
25. Draa, C. C., and Baum, H. C.: S. Clin. North America **33**: 35, 1953.
26. Cugell, D. W., Frank, N. R., Gaensler, E. A., and Badger, T. L.: Am. Rev. Tuberc. **67**: 568, 1953.
27. Patton, W. E., Abelmann, W. H., Frank, N. R., Badger, T. L., and Gaensler, E. A.: Am. Rev. Tuberc. **67**: 755, 1953.

INTERNAL PODALIC VERSION AT THE NEW YORK LYING-IN HOSPITAL (1932-1950)*

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IN HIS *Systems of Midwifery,* William Leishman, Professor of Midwifery at the University of Glasgow[1] gives some interesting details of the operation of "turning." Hippocrates, in cases of "cross-birth," advises a cephalic version whereby the head is brought to the pelvic brim. This was considered the only type of presentation feasible for delivery. Aristotle and Celsus did not agree with this teaching. DeLee[2] states that Soranus in the first century A.D. and Aetius in the sixth practiced what we regard as podalic version. He also states that Ambroise Paré practiced this form of delivery in 1550, though apparently in the interim the operation had been neglected in view of the Hippocratic dictum. In 1561, a French surgeon, Pierre Franco, in a book devoted to surgery, advised podalic version as a general operative procedure for certain conditions. In the subsequent years, this practice was continued by Guillemeau, Mauriceau, Baudelocque, and Madame La Chapelle.

The Chamberlen forceps, brought out about 1664, at once began to throw the operation of version into disfavor and as the accoucheurs became more proficient in its use they favored this over any type of operative delivery. Even as late as the end of the seventeenth century, Osiander of Strasbourg and Flamand, in view of the dangers and difficulties of the version operation, favored a return to the Hippocratic method.

While the indications for internal version were many, the contraindications were ruptured membranes, insufficient dilatation of the cervix, and contracted pelvis. It was essential that the membranes should be intact, since they kept the walls of the uterus far apart, but it was realized that the latter state of relaxation could exist even if the membranes had been ruptured for a few hours before delivery. As long as the cervix was sufficiently dilated to permit the introduction of the hand, the version could be accomplished. With regard to the contracted pelvis, Simpson, in the nineteenth century, in a very logical and forceful paper showed that a version would permit the delivery of the head with much greater ease than occurs in cephalic presentations. By means of a podalic version the bimandibular, bimalar, bimastoid and bitemporal diameters would come through the brim forming a natural wedge and permitting better molding than in cephalic presentations where the widest diameter came down first. Barnes agreed with this and illustrated by

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†Dr. Rosensohn was in poor health at the time the paper was read and subsequently died on April 26, 1953. The manuscript was not in proper form for publication, and Robert Landesman, M.D., and Frances Macdonald, A.B., prepared the manuscript and tables for publication.

a case which is quoted fully by Leishman[1] and in which the "long forceps" failed but version accomplished the delivery readily. About 1864 Braxton Hicks published his paper on podalic version and maintained that only a slight dilation of the cervix, enough to permit the introduction of one or two fingers into the uterus to grasp the lower extremities was enough. He also held that a pelvis with a true conjugate of 3 inches (7.5 cm.) was an absolute contraindication to version!

This report represents the cases in which internal podalic version was performed at the New York Lying-In Hospital from September, 1932, through 1950, a period of eighteen and one-third years. Version associated with twins is excluded. The operation was not an elective procedure for any of the patients. There was a definite indication for intervention of some type in all cases. In the period referred to there were 186 versions performed among 57,488 deliveries, an incidence of 1 in 309. The operation was accomplished about 10 times a year, the smallest number in a single year having been 4 and the largest 17. How this incidence compares with former years is shown in the report from the Bulletin of the New York Lying-In Hospital[3] of February, 1932. For a three-year period from 1929 to 1931, there were 234 versions completed in 13,447 deliveries, an average of 78 a year and an incidence of 1.7 per cent or 1 in 57 cases.

TABLE I. INTERNAL PODALIC VERSION NEW YORK LYING-IN HOSPITAL (1932-1950)

	TOTAL	PRIMIP-ARAS	MULTIP-ARAS	MATERNAL MORTALITY		INFANT MORTALITY		FULL TERM	PRE-MATURE
				NO.	%	NO.	%		
Private	104	57	47	1	1.0	12	11.5	9	3
Pavilion (ward)	82	12	70	2	2.4	34	41.5	23	11
Total	186	69	117	3	1.6	46	24.7	32	14

Table I shows the distribution among the 186 cases of version of private and pavilion patients, of primiparas and multiparas, of the maternal mortality, and of the full-term and premature infant mortality. Version was performed 104 times on the private service as against 82 on the pavilion service. In approximately 16,000 deliveries on the private service, then, the incidence was 0.6 per cent and in better than 41,000 pavilion deliveries it was 0.2 per cent. Primiparas constituted 57, or 54.8 per cent, of the private cases of version and 12, or 14.6 per cent, of the pavilion cases. The infant mortality was 11.5 per cent on the private service and 41.5 per cent on the pavilion. In the interpretation of the figures for infant deaths, the delivery procedure employed cannot be assumed to be responsible if the underlying indication was such as in itself to presume a fatal outcome. Thus, for example, 14 of the 46 infants that died were below 2,500 grams in birth weight. The marked difference in the infant death rate on the pavilion as compared with the private service may be explained in part by the preponderance of premature infants, and cases of transverse presentation, placenta previa, and prolapsed cord occurring in the pavilion series of versions. Eighty per cent of the premature infants

delivered were on the ward service and two-thirds of the patients in this series with placenta previa and transverse presentation were likewise in the pavilion category. The membranes were ruptured only a few hours or at the time of delivery in most cases, but in 8 they had been ruptured for a long time; in one instance 21 days, in another 4 days, in two others 2 days or more, and in four, 24 hours or more.

In this series of versions, three maternal deaths occurred and brief summaries follow:

1. A primipara with rheumatic heart disease and mitral stenosis was admitted to the private service in September, 1948. The pelvis was adequate. Following an average first stage of labor, forceps delivery was attempted unsuccessfully after a 2 hour second stage. Version and breech extraction were then promptly performed with the birth of a normal living infant. Bleeding was not excessive; the uterus was not ruptured. The patient went into cardiac failure and died 36 hours following delivery.

2. A multigravida was admitted in 1943 to the pavilion service with a compound presentation and premature separation. The infant was apparently dead. A labor of 32 hours with ruptured membranes for 3½ hours preceded hospitalization. A 4,240 gram macerated infant was delivered by internal podalic version. A ruptured uterus was recognized and a subtotal hysterectomy followed. Generalized peritonitis developed and the patient died on the twelfth postpartum day.

3. A multigravida with a normal pelvis was admitted to the pavilion service in 1940. After a labor of 8 hours a version was performed through a central placenta previa. A normal 2,740 gram infant was extracted. The uterus ruptured; hemorrhage occurred. Hysterectomy was performed, but maternal death resulted from hemorrhage and shock.

While these three cases represent maternal deaths, there were two private cases in which a hysterectomy was required because of ruptured uterus. Both were in multigravidas with placenta previa. In one the pelvis was normal; in the other the pelvis was borderline and the membranes were ruptured only a short time. Both patients survived. These occurred in the early years of the clinic, 1935 and 1939, respectively.

TABLE II. MORBIDITY IN VERSION

	1932 TO 1945	1946 TO 1950
Number of cases	145	41
Morbidity	31	1
Percentage	21.4	2.4

With regard to morbidity, it has been felt advisable to consider two groups, the first before and the second after the use of antibiotics. It was about 1945 that the routine use of antibiotics was started in cases in which the uterus was invaded. It will be seen from Table II that there were 31 febrile cases among 145 patients on whom version was performed when no chemotherapy had been given, and only 1 in 41 when it was administered.

With reference to hemorrhage, during or after the operation, consideration must be given to the fact that almost half the hemorrhages occurred in cases of placenta previa. Table III shows the number complicated by hemorrhage and those requiring manual extraction of the placenta. In addition to the occurrence of hemorrhage and the necessity for manual extraction of the placenta, there were 9 cases of cervical laceration and 6 cases of third degree laceration. Of incidental interest may be the observation that the largest

infants in this series weighed 5,080 and 4,670 grams, respectively, at birth, both occurring in multiparas with survival. The mother of the 4,670 gram infant sustained a ruptured uterus.

TABLE III. HEMORRHAGE AND MANUAL EXTRACTION OF THE PLACENTA

INDICATIONS FOR VERSION	HEMMORRHAGE	MANUAL EXTRACTION OF PLACENTA
Placenta previa	17	8
Transverse presentation	4	3
Occiput posterior	5	
Occiput transverse	2	1
Prolapsed cord	3	2
Prolapsed arm	1	1
Brow presentation	1	1
Face presentation	1	
Compound presentation	1	
Prolonged second stage	1	
Total	36	16

As has been noted in Table I, the infant loss was 46, of which 14 were premature. Table IV lists the injuries found in 13 of the newborn group who survived whether or not the injuries sustained were attributed to the operation of version or to some other known or unknown factors. Of these 13, injuries in 8 were of such a serious nature as to result in permanent cerebral impairment or upper extremity loss of function.

TABLE IV. INJURIES TO SURVIVING NEWBORN

TYPE OF INJURY	NUMBER	INDICATION FOR VERSION
Erb's palsy	5	1. Fetal distress
		2. Occiput posterior
		3. Transverse presentation
		4. Prolapsed cord
		5. Parietal presentation
Facial Paralysis	1	1. Occiput Posterior
Fracture	6	
Parietal		1. Occiput posterior
		2. Fetal distress
Humerus		3. Cervical dystocia
		4. Occiput posterior
		5. Placenta previa
Clavicle		6. Occiput posterior
Multiple fractures and facial palsy	1	1. Face presentation

Analysis of the cases and infant mortality according to indication for the version is shown in Table V. Where the charts indicated a transverse presentation with a prolapsed arm, the former diagnosis was used. In cases of prolapsed hand where no other presentation was noted, this was taken as the indication. It will be seen from Table V that the greatest mortality for the infant occurred in cases of transverse presentation. The 15 deaths among infants represent 40.5 per cent of the 37 cases of transverse presentation; in only one case was there a contracted pelvis. Two of 7 premature infants delivered for this indication weighed 1,580 and 1,600 grams, respectively; a third weighed 1,950 grams and the rest between 2,000 and 2,500 grams. From

this hospital in 1946, Cole and Delaney[4] reported an infant mortality of 17 per cent of 28 cases delivered per vaginam as compared with no deaths in 30 cases delivered by cesarean section. Garber and Ware[5] reported 65 cases of transverse presentation among 27,249 deliveries with a maternal mortality of 9.2 per cent and a fetal mortality of 73.8 per cent. They showed an increase to 57 per cent of cesarean section for this malpresentation in the past 6 years with no maternal deaths.

TABLE V. INDICATIONS FOR VERSION AND INFANT DEATHS

INDICATIONS	PAVILION		PRIVATE		TOTAL CASES
	NO.	INFANT DEATHS	NO.	INFANT DEATHS	
1. Occiput posterior	3	2	35	2	38
2. Transverse presentation	27	12	10	3	37
3. Placenta previa	21	9	6	1	27
4. Prolapsed cord	12	3	10	2	22
5. Occiput transverse	1	0	12	0	13
6. Fetal distress	1	1	11	0	12
7. Face	4	1	6	0	10
8. Brow	3	1	3	0	11
9. Compound presentation	4	2	1	0	5
10. Premature separation	–	–	2	1	2
11. Others	6	3	8	3	14
Total	82	34	104	12	186

Among the 27 patients with placenta previa, the infant loss was 10, or 37 per cent. Four deaths occurred with complete and 6 with partial placenta previa. Five of the 10 dead infants were premature. In 55 cases of placenta previa at this clinic from 1944-1949 which were treated by cesarean section, Landesman[6] reported only 5 infant deaths. All the 10 cases of face presentation represented full-term infants; 9 lived and one, that weighed 3,340 grams died. Brow presentation occurred in 6 cases, all full term, with one infant death in a multigravida, the baby weighing 3,970 grams. Occiput posterior and transverse position were the primary indication in 51 instances. Forty-seven living normal infants resulted. Forceps were unsuccessfully attempted in 34 cases. Associated with the version were 4 infant deaths or an 8 per cent mortality. Among the 47 living infants there were 5 injuries: fractures of clavicle, parietal bone, and humerus, facial paralysis, and Erb's palsy.

In connection with the figures and tables outlined, a comparison with the data of Jarrett and Brandenberry[7] is of interest. These authors, from the University Hospital, Cleveland, Ohio, reported a series of 448 versions in 20,017 deliveries for the years 1945 to 1949, an incidence of 2.2 per cent. This is over seven times our frequency of 0.3 per cent. These authors report a fetal mortality of 3.8 per cent without maternal mortality which is excellent. In spite of their results, these observers show a reduction in versions from 4.4 per cent in 1945 to 1.2 per cent in 1949. The low fetal mortality in internal version at the University Hospital, Cleveland, is directly related to their indications. Thirty-one and seven-tenths per cent of our versions, as compared to 2.2 per cent in the Cleveland group, were performed for prolapse

of the cord and transverse presentation. Also in the earlier years many of our versions (14 per cent), as has been indicated, were performed in the presence of placenta previa.

TABLE VI. INDICATIONS FOR VERSION IN THE UNIVERSITY HOSPITAL, CLEVELAND (1945-1949) AND NEW YORK LYING-IN HOSPITAL (1932-1950)

	UNIVERSITY HOSPITAL		NEW YORK LYING-IN HOSPITAL	
	NUMBER	PER CENT	NUMBER	PER CENT
Occiput posterior	305	85.5	38	27.4
Occiput transverse	40		13	
Occiput anterior	38		–	
Prolapsed cord	2	0.4	22	11.8
Transverse presentation	8	1.8	37	19.9
Premature separation	28	6.3	2	1.1

The technique of internal podalic version may be described as follows: much has been learned since Potter first demonstrated and described his method; this, while exemplifying nothing new, served to consolidate thoughts on details. A brief quotation may here be brought from Leishman,[1] chapter XX, page 512: "The operator should take off his coat and bare his arm so as to obviate as far as practicable any inconvenience which may arise from pressure upon the muscles. The hand and arm are liberally smeared with lard. It is generally said that to warrant an attempt at turning, the os must be dilated to the extent of a crown-piece; much argument has been wasted as to the propriety of bringing down one leg or two; the sound rule in practice is that when we succeed in securing one foot we should never pause to search for the other, nay more, the descent of one leg had a positive advantage as compared with two, as thus by increasing the diameter of the pelvis of the child, the parts are more thoroughly dilated."

Briefly, too, a word must be brought in here as to the anatomy of the pelvis, a knowledge of which will serve to facilitate the operation. In the upright position the plane of the inlet is tilted 55 degrees and the plane of the outlet 11 degrees to the horizon: the plane of the vulva is almost horizontal. A perpendicular to the plane of the inlet at its middle would go from the umbilicus to the lower end of the sacrum; this then must be the direction of the traction on the lower extremities of the fetus and on the progressive portions as they appear at the vulva. Moreover, the direction of the pull must be exerted not at right angles to the vulva but rather downward and backward practically parallel with the orifice.

As regards the operation itself, profound anesthesia is essential. Preliminary catheterization and ironing out of the perineum are important. After examination the fingers and then the hand, properly lubricated, are introduced into the vagina. The os is entered, the membranes ruptured if intact, and an attempt to grasp one or both feet made. Traction is downward and backward on the lower extremity aided by external manipulation. Displacing the head upward to the fundus will usually serve to facilitate the turning. The presenting part may be dislodged, too, by the thumb of the internal hand.

It is immaterial which hand is introduced but the one with which the operator is more expert is the better. With the appearance of the foot or feet, continued traction must be exerted above the ankle, above the knee, and above the hips favoring the turn of the infant's back anteriorly. With the birth of the umbilicus, a little cord is drawn down. As further traction is exerted, the trunk is drawn sideward until the anterior shoulder and extremity are ready for delivery. Then the body is rotated so as to deliver the other extremity anteriorly. The head may be delivered by continued traction downward and backward with the index finger of the operator in the baby's mouth causing flexion and thus permitting the suboccipitobregmatic, biparietal diameters to enter and to pass through the pelvis. Help may be obtained by an assistant exerting pressure in the hypogastrium on the fetal head or, what is better, the operator himself exerting the pressure. If there is any difficulty, forceps may be applied to the aftercoming head.

Comment

Certain conclusions may be drawn following the presentation of these statistics from the New York Lying-In Hospital. The most important of these is that the operation of internal podalic version is a serious one attended with grave potential dangers to the mother and the infant. Its employment in certain conditions in pregnancy and labor is not warranted. With the incidence in placenta previa of 10 infant deaths in 27 cases and 3 instances of ruptured uterus as well as the occurrence of 2 maternal deaths, version has no place in the treatment of this complication.

In premature separation of the placenta, though we had but 3 cases treated by version, one infant death resulted. There are many excellent reasons for resorting to cesarean section in this complication. While there were no maternal fatalities in the cases of transverse presentation, the 15 infant deaths in 37 cases should recommend strongly cesarean section for the best fetal outcome. For the malpresentations in labor, if no contraindications exist, an internal podalic version gives more satisfactory results. Even in this latter category, however, under present-day management, cesarean section is safer for the mother and the infant. The prophylactic use of antibiotics in most cases of internal podalic version is of distinct value. The rupture of the membranes is in itself no contraindication, irrespective of the time of its occurrence, as long as the uterus is not tightly contracted about the infant.

It is questionable whether internal podalic version is ever necessary at the present time in the nullipara. Rarely, in the multipara an ideal situation may present itself. Internal version may be indicated in the multipara with an adequate pelvis, intact membranes, and the cervix fully dilated. The sudden prolapse of the umbilical cord with a living infant and a dead infant in a transverse presentation are two situations in which the procedure may be indicated. These instances are indeed exceedingly rare even in a large obstetrical service.

Summary

1. The incidence of internal podalic version at the Lying-In Hospital from 1932 through 1950 was one version in 309 deliveries, which represents 10 cases per annum.

2. In all patients definite indication for termination existed; no elective versions were performed.

3. The uncorrected maternal mortality was 1.6 per cent and the infant death rate was 24.7 per cent.

4. There were 4 cases of ruptured uterus; two ended fatally and two patients recovered; all were treated by hysterectomy.

5. The patients with placenta previa and transverse presentation are best treated by cesarean section with a minimal risk for the infant as well as the mother.

6. In a few ideal cases of transverse presentation, a version may be performed with minimal risk.

7. Morbidity following podalic version is decreased by the prophylactic use of antibiotic therapy.

8. The operation of internal version is a serious one and attended with great danger to the mother and infant.

References

1. Leishman, W.: System of Midwifery, Am. ed. 2, Philadelphia, 1875, H. E. Lea.
2. DeLee, J. B.: The Principles and Practice of Obstetrics, Ed. 4. Philadelphia, 1925, W. B. Saunders Company.
3. Rosensohn, M.: Bull. New York Lying-In Hospital **13**: 361, 1932.
4. Cole, J. T., and Delaney, F.: Surg., Gynec. & Obst. **83**: 476, 1946.
5. Garber, E. C. and Ware, H. H.: AM. J. OBST. & GYNEC. **61**: 62, 1951.
6. Landesman, R.: AM. J. OBST. & GYNEC. **61**: 557, 1951.
7. Jarrett, J., and Brandenberry, K.: Surg., Gynec. & Obst. **83**: 473, 1946.

Discussion

DR. FRANK SMITH.—I cannot help on hearing this address thinking back to the pleasant years when I was house officer in the old Lying-In Hospital. Dr. Rosensohn was my first Chief of Service when I came there, which was about the time when Dr. Potter had opened the great controversy as to the elective use of versions. I felt very fortunate in having had the opportunity to experience his exact teaching for he was meticulous in his method of performing a version.

One thing that I hoped he would show in one of his slides, which he used often to emphasize was the reason why in a flat pelvis we should turn the baby and, with the finger in the mouth, bring the baby through with gentle traction. Torsion of the triangle was only increased with stronger traction.

DR. ALEXANDER H. ROSENTHAL.—Sixty-four deaths from rupture of the uterus occurred in Brooklyn during a period of about eleven years. An analysis of these 64 deaths showed what many papers in the literature have shown: namely, that the largest number of them were due to trauma, i.e., 37, and that in this group of 37 the single operative procedure which was principally responsible was version. This bears out what Dr. Rosensohn has alluded to. In 20 deaths due to version, there were 6 for placenta previa and 8 for transverse presentation. Though the cervix was not fully dilated, in the majority of cases version was followed by extraction and in all probability the

rupture of the uterus was due more to extraction than to the version itself. I think this type of experience has been responsible for causing version to fall largely into the realm of obsolete obstetric procedures.

DR. ROBERT A. MACKENZIE.—I have in the course of my years in private practice become more conservative in the use of version, but I am extremely happy that I was able to learn the technique that Dr. Rosensohn has mentioned. I have not, I think, caused women to suffer through overenthusiastic use of the intrauterine manipulation. I have confidence that, in certain cases where there is definite indication, I can employ version with success. For that reason, when Dr. Connell, in Atlantic City this year, discussed the management of obstetrical emergencies at the Margaret Hague, I felt called upon as the formal discusser of his paper to take issue with him on the use of the cesarean operation for management of transverse presentation, even with membranes ruptured for some time. I do subscribe, however, to what has been said about the bad results from the attempt to turn the baby without proper dilatation of the cervix. I certainly do not think that version has any place in the treatment of abnormal bleeding.

DR. J. EDWARD HALL.—This is the time for us to crystallize our thoughts on this procedure. In many teaching institutions it is the teaching today that version is outmoded, that it practically has no place, and, therefore, I should like to ask the speaker, what, if any, are the indications for this procedure at present?

There are certainly a great number of young men, many residents, some of whom probably never have done a version, and in whose institutions the only versions that are allowed are on the second twin and then only because the professor wants the resident to have some experience.

So I think we should ask the question, is there or is there not a place for this procedure in modern obstetrics?

DR. ROSENSOHN (Closing).—Yes, there is a place for version. One cannot say, as one of our speakers did that "a version shall never be done." One indication is that of a multigravida, at full dilatation, whose cord prolapses, in which situation cesarean is not a panacea. In a multigravida, with cervix fully dilated and a relaxed uterus with a baby not too large and in the transverse presentation, I would not hesitate to do a version. We could multiply the situations in which rather than using high forceps or resorting to a cesarean—I would do a version.

It is proper teaching which permits a version when the cervix is fully dilated, when the uterus is relaxed, when the patient is under anesthesia, when the baby is not big, and when the pelvis is normal.

PLACENTA ACCRETA

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PLACENTA accreta is a relatively uncommon complication of the third stage of labor. It is of clinical importance because it often manifests itself by severe hemorrhage. It is one of the factors making hemorrhage the leading cause of maternal mortality. A mortality rate of 37 to 67 per cent has been reported for this complication.[1]

Incidence

The reported incidence of placenta accreta shows marked variation. In Irving and Hertig's[2] series it occurred once in 1,956 deliveries; in Hirst's[3] series once in 40,000 deliveries. Undoubtedly such a discrepancy in reported incidence is due to variation in definition of this clinical entity and failure to recognize the pathologic conditions present.[4] It is probable that many cases never find their way into the literature, and that it occurs more frequently than heretofore reported. The actual incidence is estimated at 1 in 10,000 to 15,000 deliveries.

Pathology

In placenta accreta there is a pathological adherence of the placenta to the uterine wall. This results from a partial or complete absence of the decidua basalis, particularly the spongy layer. The spongy layer affords a plane of cleavage in normal implantation and has been likened to the perforations between postage stamps. When the decidua basalis is either defective or absent, the villi invade the myometrium to obtain proper nutrition for the developing conceptus, and penetrate both large and small myometrial blood vessels. There is also an increase in the number of superficial venous sinuses. This accounts for the excessive hemorrhage when the placenta is forcibly removed. The sinuses of the myometrium are exposed and in some areas there is actual hemorrhage per rhexis. Portions of the placenta accreta continue to remain attached thus preventing normal contractions of the uterus and muscular occlusion of the bleeding site.

The degree of invasion by the villi affords a pathological classification. Thus, *accreta vera* describes superficial adherence, *increta* deep penetration of the myometrium, and *percreta* complete penetration by the villi through the myometrium to the serosal surface. Another classification suggested by Reid and Aaberg[5] is based on the extent of placental involvement. If all the cot-

yledons are involved it is termed total accreta, when some are involved the condition is considered a partial accreta, and if but one cotyledon is involved it is termed focal placenta accreta.

Etiology

In general, any factors affecting decidual or placental development can result in placenta accreta. A multiplicity of etiological factors has been suggested though not all have been substantiated.[1, 4, 6, 7, 8] These many possible etiological factors may be classified as endometrial and placental. The endometrial or uterine factors include (1) prior uterine trauma from vigorous dilatation and curettage, cesarean section, myomectomy, manual removal of placenta and radiation therapy; (2) prior severe infection producing an endometritis; and (3) the presence of submucous fibroids which might prevent proper decidual reaction.

The placental factors which might favor the development of placenta accreta include (1) a poor site for implantation as seen in cases of placenta previa and in cases of bicornate uterus[7, 9, 10] (parenthetically, it is to be observed that in this congenital anomaly the incidence of accreta is relatively high), (2) developmental factors producing a placenta membranacea, and (3) retroplacental bleeding with clot formation followed by fibrosis and placenta adherence.[11]

Symptoms

Unfortunately there exist no classical or pathognomonic symptoms. Discovery is usually made during the third stage of labor. Then, separation of the placenta fails to occur and a cleavage plane cannot be found on manual exploration of the uterine cavity. The third stage of labor is usually prolonged and there is an absence of the common signs suggestive of placental separation: fundal rise, progression of the cord, and expulsion of blood. Exploration of the uterine cavity confirms the absence of the plane of cleavage and serves to differentiate true accreta from a simple retained placenta. Forceful attempts at removal can lead to inversion of the uterus or traumatic uterine rupture at the weakened placental site. Hemorrhage is a variable finding. When the adherence is complete as in total accreta, there is usually minimal or no bleeding. When the condition is partial or focal in nature, severe hemorrhage is not uncommon. The presence of placenta accreta must be considered in all cases of late postpartum bleeding, in complete abortion, and retained secundines.[1] The latter two conditions and simple incarcerated placenta are the principal entities involved in differential diagnosis. Recent reports[1, 12] indicate that a history of laborlike contractions throughout the pregnancy may be significant and should lead one to suspect the presence of accreta.

Treatment

The most accepted radical method of therapy is supravaginal hysterectomy. Mortality rates following manual extraction are reported as high as 70 per cent. Mortality rates following simple hysterectomy are less than 6

per cent.[13] Arbogast[8] reported a mortality rate of zero for cases treated by supravaginal hysterectomy directly; 18.9 per cent for cases treated by supravaginal hysterectomy following attempted manual extraction, 36.4 per cent in those cases treated by vaginal hysterectomy following attempted manual extraction, and 58.8 per cent for those cases treated by manual extraction alone. These reports seem to support the use of hysterectomy in the management of placenta accreta, particularly if the diagnosis is made at the time of cesarean section. Since the diagnosis often depends on the inability to find a cleavage plane and to remove the placenta manually, operative management is recommended for such cases, particularly in the presence of continued and severe bleeding.

Despite the reported high mortality rates there has been considerable recent support for the conservative management of placenta accreta with preservation of the uterus.[1, 8, 14-17] The patients selected for conservative management should have had minimal bleeding and minimal manipulation, and should be patients in whom future pregnancy is desired and important.

These cases are managed by the use of blood, antibiotics, oxytocics and packings. The basis for this management is the recognized success in the handling of the placenta in abdominal pregnancy. In that condition no attempt is made to remove the placenta and the umbilical cord is cut short and tied and the placenta is left attached to its original extrauterine site. Another factor influencing the decision in favor of conservative management is that placenta accreta does not necessarily recur and has been followed by normal pregnancies.[14, 16]

The danger from infection has been minimized with the advent of antibiotics. In cases of placenta accreta handled conservatively, the placenta usually sloughs away from its attachments in one to three weeks. Conservative management of partial placenta accreta necessitates removal of the bulk of the separated placenta. The possibility of choriocarcinoma developing in the retained fragments that remain attached is extremely rare after normal full-term pregnancies. McKeogh and D'Errico[1] report statistics comparable to those for immediate hysterectomy when an attempt was made at manual removal and halted if no cleavage plan could be found. These investigators are strongly opposed to routine hysterectomy without preliminary uterine examination.

Case Reports

There have been four histologically proved cases of placenta accreta at Flower and Fifth Avenue Hospitals in the period from January, 1949, to January, 1953. The incidence was 1 in 2,000 deliveries.

CASE 1.—A 30-year-old gravida iii, para ii, whose estimated date of confinement was Aug. 11, 1951, was admitted July 29, 1951, with a history of ruptured membranes and laborlike contractions for the past few hours. Her prenatal course was uneventful except for admission to the hospital in June, 1951, in false labor and eposides of repeated pain. Past history revealed the previous deliveries were by cesarean section for cephalopelvic disproportion. The patient was scheduled for immediate repeat section. At laparotomy examination of the uterus revealed fixation of the bladder flap to the old scar and dark-

blue hemorrhagic areas in the lower segment. The appearance of these areas suggested possible imminent rupture with hemorrhagic infiltration into the myometrium or adherent placenta with hemorrhagic infiltration. A low classical section was performed and a viable female infant delivered. Manual extraction of the placenta was attempted but no cleavage plane could be found even under direct visualization. A supravaginal hysterectomy was performed and the postoperative course was uneventful. Pathological report: Placenta accreta—percreta in type.

CASE 2.—A 42-year-old gravida xi, para x, was admitted on April 11, 1949, at 8:10 A.M. with a history of previously ruptured membranes, painless bright red bleeding for 6 hours. Her estimated date of confinement was March 26, 1949. Her prenatal course was uneventful. Abdominal and vaginal examination in the operating room revealed the presence of a transverse lie and a total placenta previa. Immediate cesarean section was performed and the diagnosis of placenta previa confirmed. Attempts at manual removal of the placenta were unsuccessful and a supravaginal hysterectomy was carried out. The postoperative course was uneventful and the patient was discharged on the tenth postoperative day. Pathological diagnosis: Placenta previa with accreta.

CASE 3.—A 33-year-old gravida iv, para iii, was admitted on Feb. 17, 1949, with a history of bright red vaginal bleeding of 8 hours' duration. Her estimated date of confinement was May 22. The prenatal course was marked by repeated episodes of cramplike pains and spotting. She had had a previous section for cephalopelvic disproportion. The pregnancy prior to the section was terminated by craniotomy. Her third pregnancy was delivered vaginally. The patient's bleeding became profuse soon after admission and cesarean section was performed at which time the clinical diagnosis of placenta previa was substantiated. The placenta was densely adherent to the uterine wall and all attempts at manual extraction were futile. Supravaginal hysterectomy was performed and the postoperative course was uneventful. The patient was discharged on the ninth day. Pathological diagnosis: Placenta previa with accreta.

CASE 4.—A 23-year-old gravida iv, para i, abortus ii, was admitted on Aug. 17, 1952, for repeat cesarean section. Her estimated date of confinement was Aug. 15, 1952. The prenatal course was normal. Past history revealed 2 spontaneous abortions followed by a full-term pregnancy delivered by section. A low-flap cesarean section was performed and a living 7-pound girl was delivered. Attempts at manual removal of the placenta were unsuccessful. The partially separated placenta gave rise to rather profuse bleeding and supravaginal hysterectomy was performed. The patient's postoperative course was uneventful and she was discharged on the eighth day. Pathological diagnosis: Placenta accreta—increta in type.

Comment

All four cases exhibit suggestive etiological factors. Two were associated with placenta previa, a condition characterized by implantation in an abnormal site notably poor in decidual reaction. Prior to 1950 only 21 cases of placenta accreta with previa were reported. Kistner and co-workers[7] have since reported an additional 9 cases. The addition of our 2 cases makes the total 32.

In 3 of the cases a previous section had been done and in 2 the placenta was implanted at the site of the old scar. The fourth patient had two previous abortions which might have etiological significance. Two of the patients had a history of laborlike contractions throughout the pregnancy.

In all 4 cases the diagnosis was made at the time of cesarean section. There were no suggestive symptoms since there was no third stage as follows vaginal delivery. The diagnosis was clear following attempts at manual removal under direct visualization.

The treatment in all 4 cases was supravaginal hysterectomy. The thought of conservative management was entertained. However, in view of multiparity, associated pathology, definiteness of diagnosis made at the time of section with the uterus open and under direct visualization, and failure of attempted manual extraction, it was felt that surgical management was justified. The danger of severe hemorrhage is a real one and is another factor indicating surgical management.

Summary

Placenta accreta is an infrequent complication of the third stage of labor, but the incidence is probably higher than heretofore thought with many cases either unrecognized or unreported.

While many etiological theories are propounded, endometrial inadequacy is the only one that is generally supported. This leads to faulty development of the decidua basalis with subsequent penetration by the villi and absence of the plane of cleavage.

There are no classical symptoms and in many cases, including those discussed here, the condition was discovered incidentally to section for other reasons.

Possible complications included hemorrhage, traumatic perforation of the uterus, and inversion of the uterus.

The treatment of choice is supravaginal hysterectomy. Evidence supporting conservative therapy with preservation of the uterus in the individualized case is mounting.

References

1. McKeogh, R. C., and D'Errico, E.: New England J. Med. **245**: 159, 1951.
2. Irving, F. C., and Hertig, A. T.: Surg., Gynec. & Obst. **64**: 178, 1937.
3. Hirst, B. C.: Quoted by Lawson, H. C., and Oginz, P.: Am. J. Surg. **41**: 70, 1938.
4. DeCarle, D. W.: West. J. Surg. **60**: 393, 1952.
5. Aaberg, M. E., and Reid, D. E.: Am. J. Obst. & Gynec. **49**: 368, 1945.
6. Mundt, R.: J. Internat. Coll. Surgeons **12**: 66, 1949.
7. Kistner, R. W., Hertig, A. T., and Reid, D. E.: Surg., Gynec. & Obst. **94**: 41, 1952.
8. Arbogast, P. B.: J. Indiana M. A. **43**: 111, 1950.
9. Manley, J. R.: Minnesota Med. **28**: 547, 1945.
10. Shotton, D. M., and Taylor, D. W.: J. Obst. & Gynaec. Brit. Emp. **51**: 340, 1944.
11. Hegar, A., and Maier, F.: Arch. f. path. Anat. **38**: 387, 1867.
12. Potter, M. D.: Am. J. Obst. & Gynec. **36**: 1066, 1938.
13. Cunningham, J. F.: J. Obst. & Gynaec. Brit. Emp. **49**: 149, 1942.
14. Muir, J. C.: Am. J. Obst. & Gynec. **56**: 807, 1948.
15. Smith, R. I., and Seibert, C. W.: J. A. M. A. **119**: 1417, 1942.
16. Schuman, E. A.: M. Rec. **151**: 381, 1940.
17. Kaltreider, D. F.: Bull. School Med. Univ. Maryland **30**: 1, 1945.

Department of Case Reports New Instruments, Etc.

HYDATIDIFORM MOLE OCCURRING IN ONE HORN OF BICORNUATE UTERUS

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THIS is a case report of a hydatidiform mole occurring in one horn of a bicornuate uterus. We have been able to find only one other such case in the literature.[1]

The patient was a 20-year-old white woman, para i, abortions 0, gravida ii, admitted to The Memorial Hospital at Easton, Md., Nov. 18, 1952, complaining of vaginal bleeding of two weeks' duration in the second month of pregnancy.

Her previous obstetrical history is of interest. In January, 1950, she gave birth to a 4 pound, 2 ounce infant, being delivered by breech after a pregnancy of 32 weeks. Her physician at that time did not determine that she had a bicornuate uterus.

On the present admission she stated that her last menstrual period had been Sept. 15, 1952. On November 4 she started to bleed vaginally following a tooth extraction. During the following two weeks she continued to bleed moderately but had no cramps and did not recognize any products of conception.

Physical examination on admission showed a healthy young white woman in no distress. Temperature, pulse, respirations, and blood pressure were normal. Abdominal and pelvic examinations revealed a tender mass in the right adnexal region, 3 inches in diameter, in direct continuity with what was considered to be a slightly enlarged, midline, uterine fundus. There was a small amount of blood in the vaginal canal.

Laboratory examinations showed a red blood count of 3.5 million with a hemoglobin concentration of 10.2 Gm. per 100 c.c., or 70 per cent. The hematocrit was 32 mm. The platelet count was 210,000 per cubic millimeter. The white blood count was 8,600 with a normal differential. The urine was normal.

Because of the presumptive diagnosis of a right tubal pregnancy she was taken to the operating room where a double setup had been prepared. Examination under anesthesia confirmed the previous finding of a right adnexal mass adjacent to an essentially normal-sized midline uterus. The uterus was sounded 10 cm. in the midline. Dilatation and curettage yielded 2 c.c. of succulent material which on frozen section showed a decidual reaction, but no chorionic villi or other trophoblastic elements were found. After proper cleanup and draping, the abdomen was opened through a lower midline incision. It was found that she had a bicornuate uterus with a normal tube and ovary on each side. The right horn of this uterus measured 3½ inches in its greatest diameter and its color and consistency were indicative of pregnancy. The left horn was a normal-sized fundus in the midline, a small appendage to the enlarged right horn. The kidneys were normal. The vermiform appendix was removed and the abdomen closed.

The patient recovered from the operation promptly. She was started on diethylstilbestrol, 5 mg. daily, progesterone 10 mg. daily, and desiccated thyroid, ½ grain twice daily.

Twenty-four hours after operation she expelled 100 c.c. of material recognized grossly and microscopically as a hydatidiform mole. Because of this she was returned to the operating room 10 days later for curettage. A probe passed through the external cervical os into a single canal approximately 1½ cm. in length. Above this the probe could be passed into the right or left horns and the septum between the two appeared to be everywhere intact. The right, or previously pregnant cavity, was curetted of a teaspoonful of material which on subsequent microscopic examination showed actively proliferating trophoblasts. She has remained well since. *Rana pipiens* tests have been negative for chorionic gonadotropic hormone.

Comment

Hydatidiform mole occurs about once in every 2,000 uterine pregnancies. The cause is not known. It would appear to be either a defect in the ovum or a defect in the maternal environment provided for the ovum. In support of the opinion that an ovum defect is responsible are the reports[2-5] of double ovum twins in which one ovum is a mole and the other a normal fetus. That the ovum defect is not incompatible with a normal fetus is shown by the reports[6-9] of single pregnancies in which a mole is associated with a living child. Some of these children had congenital defects. In support of the opinion that the environment provided for the ovum is at fault are the reports[10-14] of numerous instances of hydatiform degeneration in tubal pregnancies. The abnormality has even been described in ectopic ovarian pregnancy.[15] The case herein reported is one in which the maternal environment provided for the ovum would appear to be at fault. The follow-up, with uterosalpingography, of patients who expel moles may reveal more uterine abnormalities than was previously suspected.

Summary

1. A case of an hydatidiform mole occurring in one horn of a bicornuate uterus is reported. Only one similar case has been found in the literature.

2. Instances of unusual moles are cited in support of the various theories concerning the cause of hydatidiform moles.

References

1. Deutschman, D.: Bulletin Russian M. Soc., New York, September, 1939, pp. 109-112.
2. Falgowski, E.: Monatschr. für Geburtsh. u. Gynäk. **34**: 290, 1911.
3. Lukens, G.: Proc. Roy. Soc. Med. (Obstetrical and Gynaecological Section) **7**: 113, 1914.
4. Mishler, H. V., and Dickerhoof, G. R.: Ohio State M. J. **44**: 714, 1948.
5. Waters, E. G., and Crunden, A. B.: AM. J. OBST. & GYNEC. **46**: 299, 1943.
6. Thaisz, K.: Zentralbl. f. Gynäk. **62**: 1937, 1938.
7. Mueller, C. W., and Lapp, W. A.: New York State J. Med. **50**: 1279, 1950.
8. Chacko, A.: Indian M. Gaz. **78**: 95, 1943.
9. Bowles, H. E.: AM. J. OBST. & GYNEC. **46**: 154, 1943.
10. Meyer, A. W.: Surg., Gynec. & Obst. **28**: 293, 1919.
11. Pettit, M. DeW.: AM. J. OBST. & GYNEC. **42**: 1057, 1941.
12. Medina, J., Gallucci, J., and Amorim, M.: An. brasil. de ginec. **18**: 337, 1944.
13. Hückel, R.: Centralbl. f. allg. Path. u. path. Anat. **41**: 434, 1928.
14. Sherman, J. T.: Am. J. Surg. **27**: 237, 1935.
15. Stander, H. J.: Williams Obstetrics, ed. 8, New York, 1941, D. Appleton-Century Company, p. 729.

TORSION OF A TUBE AND OVARY COMPLICATING PREGNANCY: REPORT OF TWO CASES

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THE rarity of torsion of the adnexa complicating pregnancy is evidenced by the paucity of information found in the standard textbooks on obstetrics and gynecology. From time to time in the literature, there are case reports of the torsion of a normal tube or normal ovary complicating pregnancy, but there are even fewer reports of torsion of a normal tube and ovary together complicating pregnancy. Because of the unusual occurrence of this condition I feel it is worth reporting two cases which have recently come under my care.

CASE 1.—Mrs. S. W. (Col. Hosp. No. 152132), a 26-year-old housewife, was first seen on March 7, 1952, and stated that her last menstrual period had been on Jan. 2, 1952. Her estimated date of confinement was Oct. 9, 1952. Past history revealed an appendectomy in 1945, hymenectomy in 1946, and pleurisy in 1949. She had been delivered of a 6 pound, 13 ounce male infant in 1948 after a twelve-hour labor. Physical examination was essentially normal. She was Rh positive, Wassermann negative, the urinalysis and blood count were normal. The pelvic measurements were clinically adequate. The pregnancy was uneventful until 5 P.M. on July 7, when she had a sudden onset of severe pain in the left lower quadrant of the abdomen, which persisted in spite of codeine and Demerol. She was admitted to the hospital at 1:45 A.M. July 8, 1952. Examination at this time revealed her to be in a great deal of distress. The abdomen contained a pregnant uterus enlarged to six months' size. The fetal heart was heard on the right side of the abdomen. There was extreme tenderness in the left lower quadrant to light touch; no rigidity, no rebound tenderness, and no masses were felt. No masses were felt by rectal examination. The temperature was 98° F., pulse 84, respirations 18, and blood pressure 110/70. A catheterized urine specimen and blood count were perfectly normal. The white blood count was 8,000 with a normal differential count. There were no urinary symptoms. The patient was well sedated but there was no relief in the amount of pain present in the left lower quadrant. A flat plate of the abdomen revealed a single fetus in the breech position. An intravenous pyelogram revealed normal findings in a patient six months pregnant. There were no calculi seen. The pain persisted in a localized area of the left lower quadrant. For the next three days the temperature, pulse, respirations, blood pressure, urinalyses, and blood counts remained essentially unchanged from the time of her admission. On July 11, 1952, intermittent uterine contractions started and a tentative diagnosis of torsion of the left adnexa was made and laparotomy was advised. A left pararectus incision was made, and when the peritoneal cavity was entered it was seen that the left ovary and Fallopian tube were completely twisted one and a half times. The left ovary was gangrenous and two-thirds of the left tube was gangrenous with thrombosis of the vessels extending into the left infundibulopelvic ligament. A left salpingo-oophorectomy was performed. The pathological report was acute hemorrhagic necrosis of the tube and ovary. The postoperative course was uneventful and the patient was discharged on the ninth postoperative day. The remainder of the pregnancy was not remarkable and the patient delivered a 7 pound male infant on Oct. 2, 1952, after a six-hour labor.

CASE 2.—Mrs. C. L. (P.G.G.H. No. 44059), a 20-year-old housewife, para 0, gravida i, was first seen by me on April 13, 1953, in consultation. Her last menstrual period was on Aug. 18, 1952, and her estimated date of confinement was May 25, 1953. There had been no previous illnesses or operations. Her prenatal course was normal until 8:30 A.M. on April 11, 1953, when she started to have cramplike pains in the lower abdomen. She stated that she had had the same kind of pains in the third month of pregnancy in the left lower quadrant for about one-half hour but that they had disappeared spontaneously. The pains persisted throughout April 11, 12, and 13, along with nausea but no vomiting. They became rather severe and localized in the left lower quadrant. On examination the temperature was 98.8° F., pulse 90, and respirations 20. The abdomen was enlarged to the size of a 7½ months' pregnancy. The fetal heart was heard in the right lower quadrant. The uterus was very tender throughout and was contracting irregularly. There were severe localized pain and tenderness in the left lower quadrant with rebound tenderness. No masses could be felt. Rectal examination was negative. Blood pressure was 115/68, a catheterized urine specimen was negative, and the blood picture showed 4.18 million red blood cells, 15,800 white blood cells, and a normal differential count. A diagnosis of torsion of the left adnexa was made and laparotomy advised. A left pararectus incision was made and on opening the abdomen it was seen that the left tube and ovary were necrotic and hemorrhagic, and completely twisted at the cornual end of the tube. A left salpingo-oophorectomy was performed. The pathologist reported acute hemorrhagic necrosis of the left tube and ovary. The postoperative course was notable only for minimal distention, relieved by the insertion of a Levine tube for 48 hours. The patient was discharged on the eighth postoperative day and readmitted on May 25, 1953, when she delivered a six pound, 12 ounce male infant spontaneously after a nine-hour labor.

Comment

Two cases involving torsion of the left adnexa complicating the middle and last trimesters of pregnancy are reported. Both cases were characterized by sudden onset of severe pain in the left lower quadrant of the abdomen, without any change in the temperature, pulse, blood counts, or urinalyses, nor were any pelvic masses felt.

Disease of genitourinary origin such as calculi, Dietl's crisis, etc., must be considered in the differential diagnosis. Laparotomy must be performed as soon as the diagnosis of torsion is made or suspected, as the necrotic tissue and subsequent absorption of toxins will soon cause uterine contractions and subsequent labor. Both of these patients developed uterine contractions but they quickly subsided as soon as the offending tissue was removed, and the pregnancies were carried to term.

2025 EYE ST., N. W.

MESONEPHROMA OF THE OVARY

Report of a Case

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(From the Gynecological Department of the Columbus Hospital)

In 1939, Schiller described an ovarian tumor which he thought should be differentiated from the known ovarian tumors, for its unusual morphological pattern. Microscopically, this tumor revealed some peculiar formations, which strongly resembled fetal glomeruli, and, on this finding, Schiller thought the tumor was derived from the mesonephron and called it mesonephroma. After Schiller's original report, numerous further cases of mesonephroma have been reported by different authors: Jones and Seegar in 1940, Kazancigil, Laqueur, and Ladewig in the same year, Tuta and Siebel in 1941, Rosenblatt and Grayzel, and again Jones and Seegar Jones in 1942, and in 1943, Stromme and Traut, Schornagel, and Da Silva Fialho. Recently, Nora and Baserga also reported a case of mesonephroma.

A complete review of the literature concerning mesonephroma is given in the paper by Nora and Baserga, to which we refer. They collected a total of 43 cases registered in the literature, excluding the cases of mesonephroma located in the testicle (Kazancigil and associates, Teilum). Most of the cases have been reported in America, with the exception of three cases reported in Turkey by Kazancigil and co-workers and a case described in Holland by Schornagel.

However, Nora and Baserga pointed out that quite a few cases reported in the literature as mesonephromas do not fulfill the features indicated by Schiller as diagnostic of this tumor. According to Schiller, there is, in the mesonephroma, "a structural unity definitely characteristic and specific. This unit is represented by small cavities, each of which contains only one relatively large papillary projection . . . lined, and similarly the cystic cavity is lined, with an endothelium-like covering." These formations allow a differential diagnosis from the serous papillary cystadenoma, because the cystic cavities are smaller, lined by a bulging endothelium, and contain a single papillary projection with scanty connective tissue and a large capillary, while, in the common cystadenoma, the cystic cavities are larger and contain numerous papillary projections with an ample connective core and many small capillaries.

This unit is the only one that should permit a diagnosis of mesonephroma. However, there is another feature which is characteristic, although not

specific, of this tumor, and this is a large cavity containing one or more papillary projections made up of a single layer of large bulging cells, arranged like a crown around an ample capillary. This picture is not specific, but it is quite common in mesonephroma, as has been reported by Schiller and emphasized by Nora and Baserga. If the diagnosis of mesonephroma is restricted to the cases which present the above-mentioned characteristic units, quite a few cases registered in the literature must be discarded. According to Nora and Baserga, the following cases reported by the different authors do not fulfill the requirements indicated by Schiller for the diagnosis of mesonephroma: the fifth case in Schiller's original report (personal communication), the last three cases described by Jones and Seegar in 1940, the second case by Kazancigil, Laqueur, and Ladewig, the nine cases reported by Jones and Seegar Jones in 1942, and nine out of the ten cases reported by Stromme and Traut, the only one fulfilling the requirements of mesonephroma being the fourth case. The other nine cases showed an epithelium giving the staining reaction of mucin, while, according to Schiller, one of the most important features of mesonephroma is that its cells are not mucus producing.

If these cases are discarded, only twenty-one cases are left recorded in the literature; namely, nine cases in Schiller's original report, three cases by Jones and Seegar, two cases by Kazancigil, Laqueur, and Ladewig, two cases by Da Silva Fialho, and the single cases described by Tuta and Siebel, Rosenblatt and Grayzel, Stromme and Traut, Schornagel, and Nora and Baserga. These cases, for the microscopic description and for the pictures presented, can be easily identified as a distinct, well-differentiated entity, i.e., the mesonephroma. The typical architectural pattern of these tumors permits them to be differentiated from any other known ovarian tumor, and it is our opinion that, if the specific features are kept in mind, nobody can question the existence of the mesonephroma as a pathological entity, as Jones and Seegar had already pointed out: "Whatever may be the ultimate fate of mesonephroma in the scheme of ovarian tumors, especially as regards its histogenesis, there can be little doubt that it is a pathological unity."

As far as the biological activity of this tumor is concerned, nine out of the twenty-one cases of the literature accepted by us must be considered malignant, as demonstrated by the presence of metastases; namely, four cases by Schiller, two cases by Jones and Seegar, the first case by Da Silva Fialho, and the cases by Tuta and Siebel, and Rosenblatt and Grayzel. In addition, two further cases reported by Schiller appear to be uncertain. Particularly interesting is the fourth case reported by Schiller in a baby girl of 8 months of age, in which the mesonephroma appeared as a growth protruding from the vagina, and the primary site of the tumor could not be established. In reviewing the literature, we found a case, which has not been mentioned by Nora and Baserga, and which has been reported by Nicholson in his book, *Studies on Tumour Formation*. Fig. 51 on page 93 of Nicholson's book represents a typical mesonephroma, a strikingly similar picture having been

published by Schiller on page 448 of the *Archives of Pathology,* volume 33, year 1942. The tissue illustrated in Nicholson's book was removed for histological examination from the vagina of a woman of 64. She died a few days later and only a local examination was allowed. The vault of the vagina was occupied by an ulcerated new growth, which extended around the whole of its circumference to about the middle. The tumor had invaded the cervix uteri, the remains of which were present in its upper part. The external os was recognizable, and the cervical canal was patent, although its walls were covered by the growth. This extended to the level of the internal os, the body of the uterus being free from it. There was extensive infiltration of the base of the broad ligaments, especially on the left side. Unfortunately, according to Nicholson, the disease was too far advanced to have revealed on examination the part in which it originated. It seems to us that this case reported by Nicholson resembles the fourth case described by Schiller. Actually, Nicholson claimed that this was a papillary carcinoma arising from the ampulla of Gartner's duct, but, as we mentioned above, the picture shows the typical pattern of a mesonephroma, and it would not be impossible that the real site of the primary tumor was located in the broad ligament. As a matter of fact, Nicholson himself states, about this tumor, that "it is clearly built up on the same plan as the broad ligament cyst in Fig. 50." We therefore feel no hesitation in claiming that this tumor described by Nicholson is a mesonephroma, most likely arising from the left broad ligament, and infiltrating the cervix uteri and the vagina, as in the fourth case by Schiller. Due to its high infiltrating activity, this tumor must be considered the tenth case of malignant mesonephroma in the literature, out of a total of 22 cases accepted by us as true mesonephromas.

As far as the localization is concerned of these 22 cases, eleven were located in the right ovarian region, six in the left, and in five cases the primary site of the growth could not be established. The age does not seem to have any importance: cases have been described in a baby girl of 8 months of age (Schiller) and in a woman of 63 years (Jones and Seegar), while in the case of Nicholson the woman was 64.

The pathogenesis of the tumor is a matter of discussion. As we mentioned before, Schiller, on the basis of his histological findings, especially the findings of the glomerular bodies and glomerulus-like structures, thought the tumor was derived from the primitive mesonephron. In a second report, Schiller presented a tumor located in the kidney, the histological pattern of which showed no difference from the picture of the ovarian mesonephroma. However, most of the authors do not agree with Schiller about the origin of this tumor. Kazancigil and co-workers claimed that there was no resemblance between the papillary projections of the mesonephroma and a fetal glomerulus, and they called the tumor in question "papillo-endothelioma ovari." Stromme and Traut also denied its mesonephric origin and called the tumor "teratoid adenocystoma of the ovary." On the other side, Jones and Seegar claim that Schiller's hypothesis cannot be discarded; however, it is their

opinion that, up to date, only the dysontogenetic origin of the tumor can be considered as proved. We definitely agree with Jones and Seegar. At least, five cases have been described in which the mesonephroma was associated with teratoid structures, two by Schiller, two by Kazancigil and collaborators and one by Nora and Baserga. A further proof of the dysontogenetic origin of this tumor is the fact that it has been described, not only in the ovary, but also in the testicle (Kazancigil and co-workers, Teilum) and in the kidney (Schiller). We therefore believe that the mesonephroma is a dysontogenetic tumor and, though its strictly mesonephric origin has not yet been proved, we are of the opinion that the name of mesonephroma should be maintained until a more adequate name will be proposed.

The case we are going to report must be considered the twenty-third case of mesonephroma registered in the literature, the true nature of which has been histologically supported.

Case Report

Miss J. H., a white woman, 45 years of age, was admitted to Columbus Hospital on Sept. 5, 1952, complaining of some discomfort and tension on the left side of the abdomen. She had been examined a few weeks before and a vague diagnosis of "tumor" had been made. Menstruation had been regular until one year before; since then the period came regularly every two months. The last menstrual period was in the last week of August. Her past history was completely negative, except for a tonsillectomy in childhood.

On physical examination, the abdomen was found to be quite distended. There was some tenderness in the left lower quadrant, where a large mass, extending toward the center of the abdomen, was palpable. The mass was the size of a pineapple and had an upper convexity at the level of the umbilical line.

On admission, the white blood cell count was 9,850, the red blood cell count 3,620,000, and the hemoglobin was 59 per cent. The differential count gave 76 neutrophils, 15 lymphocytes, and 9 monocytes. Urine analysis was negative, except for occasional white blood cells and epithelial cells in the sediment. The Kahn test was negative.

The patient was operated upon on Sept. 6, 1952. There was a large amount of blood-tinged fluid in the peritoneal cavity. The left ovary was cystic. There were areas of firmness, the largest of them about 4 to 5 cm. in diameter, and firmly attached to the bowel. The right ovary was also enlarged and firm. The omentum was thickened and nodular. There were many adhesions from the liver to the diaphragm. The liver was palpably smooth. A biopsy of the left ovary and omentum were taken. The patient left the operating room in good condition. The postoperative course was uneventful and the patient was discharged on 9-17-1952.

Microscopic Examination: The ovarian specimen appeared to be made up of several cystic cavities of different size. These cavities were separated by broad strands of connective tissue, rather dense and uniform. The cystic cavities were lined by a single layer of closely packed cells, with large round nuclei and scanty vacuolated cytoplasm. The cells were bulging into the lumen and showed a slight irregularity in size and shape. The most important feature, however, was the presence of papillary projections in the lumen of the cystic cavities. Some of the cavities contained many papillary projections, others only a few. There were some consisting of a single ample capillary vessel (Fig. 1) covered by a crownlike layer of cells with the same characteristics as the cells lining the cystic cavities. In some places, however, few typical glomerulus-like formations were seen (Fig. 2). They consisted of a single papillary projection arising from the cyst's wall and made up of an ample capillary covered by closely packed cells with large round nuclei and scanty vacuolated cytoplasm. These structures definitely resembled the glomerular bodies described by Schiller; however, the lining cells were slightly irregular

in size, and some of them were also hyperchromatic. A careful examination revealed few mitotic figures. With van Gieson staining, the broad strands of connective tissue stained a faint pink, while the papillary projections took a very light yellow, and the nuclei stained deeply with the iron hematoxylin.

The biopsy of the omentum revealed similar changes: the omentum was invaded by tumor tissue with the same characteristics described above. However, in some places,

Fig. 1.

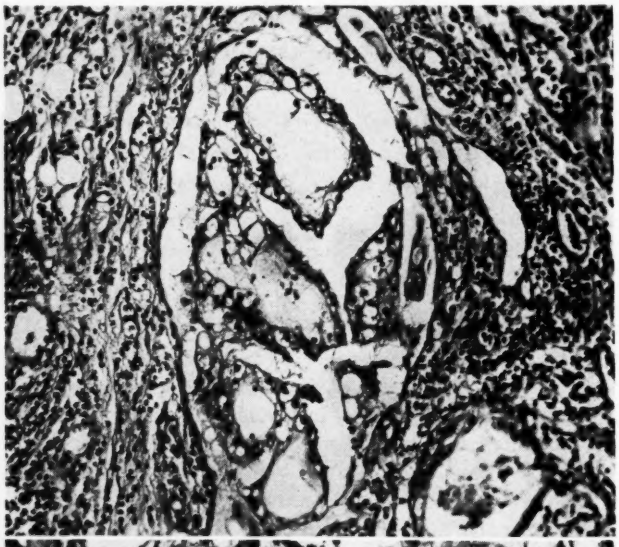

Fig. 2.

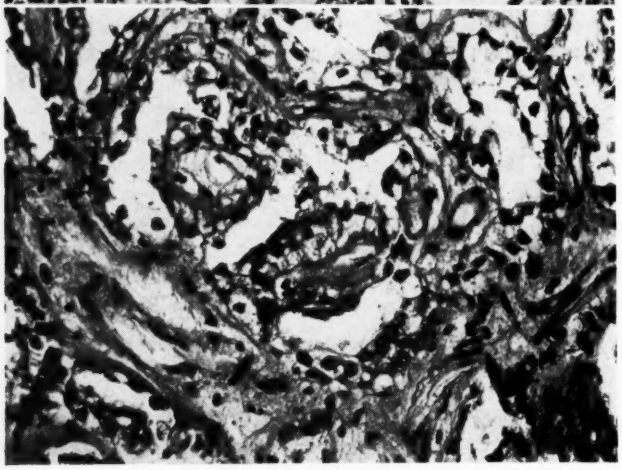

Fig. 1.—Metastasis of mesonephroma in the omentum. (×200. Reduced two-fifths.)

Fig. 2.—Pseudoglomerular formations of mesonephroma specimen taken by the primary growth. (×400. Reduced two-fifths.)

deposits of calcium were found in the papillary projections: the cells were markedly vacuolated, even more than in the primary tumor. There was a rather dense lymphocytic and plasmacytic exudation around the islands of tumor tissue.

Diagnosis: Malignant mesonephroma of the ovary metastatic to the omentum.

Conclusions

A case of malignant mesonephroma of the ovary metastatic to the omentum has been reported. If the histological features indicated by Schiller are kept in mind, several cases described in the literature as mesonephromas have to be discarded, and this would be only the twenty-third case of ovarian mesonephroma, whose true nature has been proved through histological description and photomicrographs. In eleven instances out of these 23 cases, the mesonephroma appeared to be malignant, as proved by the presence of metastases.

We agree with most of the authors that the mesonephroma must be considered as a distinct pathological entity, well separated from the other known ovarian tumors. On the other hand, the pathogenesis of this tumor is still open to discussion.

References

1. Da Silva Fialho, A.: An. brasil. de ginec. **15**: 3, 1943.
2. Jones, W. H., and Seegar, G. E.: Am. J. Obst. & Gynec. **39**: 322, 1940.
3. Jones, W. H., and Jones, G. E. Seegar: Arch. Path. **33**: 18, 1942.
4. Kazancigil, T. R., Laqueur, W., and Ladewig, P.: Am. J. Cancer **40**: 199, 1940.
5. Nicholson, G. W. de P.: Studies on Tumour Formation, St. Louis, 1950, The C. V. Mosby Company.
6. Nora, E., and Baserga, R.: Riv. anat. pat. e onc. **6**: 987, 1953.
7. Rosenblatt, P., and Grayzel, D. M.: Am. J. Obst. & Gynec. **43**: 116, 1942.
8. Schiller, W.: Am. J. Cancer **35**: 1, 1939; Arch. Path. **33**: 443, 1942.
9. Schornagel, H. E.: Nederl. tijdschr. v. geneesk. **87**: 989, 1943.
10. Stromme, W. B., and Traut, H. F.: Surg., Gynec. & Obst. **76**: 293, 1943.
11. Teilum, G.: Acta path. et microbiol. scandinav. **23**: 242, 1946; **27**: 249, 1950.
12. Tuta, J. A., and Siebel, J. E.: Arch. Path. **31**: 386, 1941.

CERVICAL PREGNANCY

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CERVICAL pregnancy may be defined as an ectopic gestation in which implantation and development of the fertilized ovum take place in the cervix.

Since there have been a considerable number of papers in recent years dealing with this subject, this report will deal primarily with a case presentation of what appeared to be a cervical pregnancy, followed by two normal pregnancies in the same patient.

Case Report

J. C., No. 102196, aged 21 years, white, gravida i, para 0, was first seen in my office on Sept. 9, 1950, because she suspected she might be pregnant. Her last menstrual period was July 2, 1950, giving her an estimated date of confinement of April 9, 1951. Her past history was clinically irrelevant. Menses began at 12 years, occurring every twenty-eight to thirty days and lasting for four to five days. Examination revealed a slender, healthy young woman who showed no evidence of abnormality. The heart and lungs were negative. The breasts were tense and showed evidence of early pregnancy. The abdomen was negative. Pelvic examination revealed a softened bluish cervix, slightly eroded, through which a small polyp or piece of decidual tissue could be seen. The uterus was slightly enlarged, soft, and anterior. The adnexa revealed no significant abnormality. Laboratory findings were essentially within normal limits. Impression at this time was that of uterine pregnancy with possible cervical polyp.

Re-examination on Sept. 16, 1950, one week later, revealed that the tissue extruding from the cervical os was definitely a polyp.

On Sept. 30, 1950, she complained of sharp intermittent pain in both lower quadrants, especially on the right side and in the pelvis and of difficulty with the bowels, more in the nature of painful constipation.

On Oct. 17, 1950, low abdominal discomfort became markedly aggravated and she was forced to stay in bed. No bleeding was noted. She still had bowel difficulty.

On Oct. 27, 1950, slight vaginal bleeding occurred, accompanied by low abdominal cramps and pelvic discomfort. The patient was hospitalized at Toledo Hospital and placed on a routine threatened abortion regime. All bleeding then ceased and the vaginal discharge became brownish in nature. The treatment consisted of bed rest, sedation, and large doses of stilbestrol.

On Oct. 31, 1950, vaginal bleeding increased, low abdominal cramps with a sensation of pressure became worse, and rectal tenesmus became the main complaint. Abdominal examination revealed the fundus to be halfway up to the umbilicus. However, it did not seem as wide as one would expect it to be. A sterile vaginal examination was then done and it was noted that the cervix was completely distended, thinned out, and seemed to fill the entire pelvis. The external os was the size of a pin point and a small amount of brownish discharge was coming out of it. On digital examination the cervix felt as smooth as a billiard ball and appeared to be pressing against the rectum. (This was probably the cause for the tenesmus.) This cervical mass was thought at that time to be contiguous with the uterus. It was felt that we were dealing with an inevitable abortion.

Approximately six hours after the examination the patient had a small hemorrhage, losing several hundred cubic centimeters of blood, followed two hours later by another hemorrhage of about 200 c.c. Whole blood, 500 c.c., was given at that time. The blood was of improper type. She was given Rh-positive group O blood, and the patient was in group B. A moderate transfusion reaction occurred with resultant hematuria.

A repeat examination at that time showed that the cervix was beginning to dilate. Bleeding was not too profuse and it was decided to leave the patient alone overnight. The following morning, Nov. 1, 1950, the patient expelled a fetus of about three and one-half months' gestation. Examination of the placenta revealed it to be incomplete. Bleeding continued to be very profuse and a curettage was decided upon. This was performed approximately four hours later.

Under Pentothal Sodium anesthesia, with the patient receiving whole blood, the vagina was prepared. A speculum was placed in the vagina and the following were noted: The cervix was thin, the edges ragged, the walls grayish and very friable. Attempts to grasp the cervix failed on several occasions because of the friability of the tissue involved. It had the appearance of a cervix following a difficult vaginal delivery at term. The walls of the sacculated cervix were covered with placental tissue and the entire cavity had the appearance of a dome at the apex of which was an aperture about 2 cm. in diameter and leading into the corpus uteri. The diameter at the widest point was about 6 cm. and the depth of this cervical cavity was estimated at about 5 to 6 cm. Placental tissue was removed from the walls of the cervix by digital and blunt instrumental curettage. Bleeding from the open sinuses became so profuse that the entire operative field quickly became a bloody lake. The patient went into shock. The entire area was quickly and very tightly packed with plain gauze and the patient received 1,000 c.c. of whole blood on the table, under forced pressure, within a period of seven to ten minutes. It was estimated that she must have lost about 1,000 c.c. of blood within a few minutes. During the operative process, the cervix was torn in several places requiring mattress sutures. After the blood was given, the patient was returned to her room in fair condition and placed on antibiotic and other supportive treatment, including additional blood.

Her postoperative course was uneventful. The pack was removed slowly in stages, on the second postoperative day, and she was discharged from the hospital on the eighth postoperative day without any complaints and with a normal vaginal lochia. A checkup at three and six weeks after the operation revealed an essentially normal pelvis with the exception of slight cervical scarring.

This patient was again seen on July 21, 1951, and a diagnosis of intrauterine pregnancy was made with the estimated date of confinement March 12, 1952. Her pregnancy was uneventful and she was delivered of a live female infant, March 8, 1952, after a four-hour labor. Examination of the cervix at that time revealed it to be paper-thin and in some areas it had a "bluish-gray" translucency.

Postpartum checkup six weeks later revealed essentially normal pelvic findings with the exception of notching in the anterior lip of the cervix.

On April 8, 1953, she was again delivered of a normal female infant after an uneventful pregnancy and a very short labor. Postpartum findings were essentially the same as before.

Summary

1. A case of probable cervical pregnancy, which was followed by two normal pregnancies, is presented and discussed. This case fits the description of some of the pathologically proved cases described in the literature.

2. A few of the clinical high lights are presented. These consisted of extreme low abdominal and pelvic visceral discomfort, almost constant, as well as rectal tenesmus associated with severe constipation. Bleeding at first was rather slight. The apparent ballooning and distention of the cervix to an extent that it filled the pelvis was suggestive of this condition.

3. Whenever possible, we should refrain from removing the placental tissue from the wall of the cervix and we should pack tightly against the cervix to control bleeding. The pack should be removed gradually. Blood in large quantities must be available at a moment's notice. The patient should receive whole blood during the entire operative procedure.

4. Conservative treatment should be employed whenever possible, for these women may become pregnant and subsequently may deliver without difficulty.

5. The existence of this rare form of ectopic pregnancy must be kept in mind. One must remember that the key to successful management in these cases is prompt control of bleeding and rapid replacement of blood by means of whole-blood transfusions.

SPONTANEOUS INTRAPERITONEAL HEMORRHAGE DURING PREGNANCY

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SPONTANEOUS intraperitoneal hemorrhage, referred to as "abdominal apoplexy" by some authors, is a very uncommon occurrence, and extremely rare in connection with normal intrauterine pregnancy.

In a very comprehensive review of the literature in 1947, Tanna[1] found 32 cases of spontaneous intra-abdominal hemorrhage and added 3 more cases. Of these 35 cases, 25 were men and 10 were women. There was no mention made of the coexistence of pregnancy in any of the women, and none of them were reported in any of the obstetrical journals. The ages of these 35 patients ranged from 27 to 83 years, with the greatest frequency of occurrence being in the sixth decade. In 15 of the cases no definite bleeding point could be found, and all of these cases occurred in the younger individuals in the group, and, incidentally, they had the highest mortality rate (33⅓ per cent). The majority of the 35 patients had hypertension and/or arteriosclerosis.

In 1949 Sharp and Horton[2] reported a case of abdominal apoplexy which occurred in a 24-year-old married nonpregnant woman. They were unable to locate the bleeding point, but the patient recovered uneventfully after operation.

In 1950 Darling[3] reported a case of intraperitoneal hemorrhage occurring in a 73-year-old white man with cardiovascular disease. The bleeding came from a spontaneously ruptured branch of the right colic artery, and the patient recovered after the vessel was ligated.

Ross[4] reported a case of abdominal apoplexy occurring in a 61-year-old white man with hypertension and arteriosclerosis due to a spontaneous rupture in a cecal branch of the ileocolic artery, and complicated by postoperative mesenteric thrombosis and an *Escherichia coli* empyema of the left pleural cavity. The patient recovered following bowel resection and drainage of the empyema.

In 1951 Becker[5] reported a case of spontaneous rupture of a branch of the superior mesenteric artery causing massive intraperitoneal hemorrhage in a 39-year-old white man. The patient had essential hypertension, and the episode of abdominal apoplexy occurred on his fourth postoperative day following a left thoracolumbar sympathectomy. The diagnosis of massive intraperitoneal hemorrhage was made and laparotomy was performed with ligation of the bleeding vessel and resection of a gangrenous segment of jejunum. Five days later the patient suddenly died, and at autopsy death was found to have been due to coronary occlusion and myocardial infarction.

Hahn[6] recently reported a case of abdominal apoplexy occurring in a 45-year-old married Negro woman, gravida v, para v. A preoperative diagnosis

of intra-abdominal hemorrhage probably due to a ruptured ovarian cyst was made, and, at laparotomy, hemoperitoneum due to a rupture in the mid-colic artery was found. The artery was ligated, and the patient made an uneventful recovery.

There have been over 100 cases reported in the literature of spontaneous retroperitoneal hemorrhage during pregnancy, in some of which there was secondary intraperitoneal hemorrhage due to the extravasated blood breaking through the peritoneum into the abdominal cavity, but, to my knowledge, this is the first case reported of spontaneous primary intraperitoneal hemorrhage during normal intrauterine pregnancy.

Case Report

A 30-year-old white housewife, gravida iv, para iii, was admitted to Scripps Memorial Hospital at 8:15 P.M., Sept. 16, 1952, with the chief complaint of lower abdominal pain. Her last menstrual period had begun on March 3, 1952, and she had had a normal prenatal course until the day of admission when she gradually developed epigastric pain, which soon shifted to the right lower quadrant, and was associated with nausea and vomiting. Her three previous pregnancies had been normal except for excessive bleeding about one hour after delivery of her third child, at which time she was given intravenous oxytocics and 1,000 c.c. of whole blood.

Positive physical findings on admission were (1) a uterus of the size of a six and one-half months' pregnancy but not firm or tender, (2) normal fetal heart tones, (3) tenderness in the right lower quadrant of the abdomen with some voluntary muscle "guarding" but no rigidity, and (4) temperature 99.2° F., pulse 96, respiration 22, and blood pressure 110/70. Laboratory tests showed a hemoglobin of 8.7 Gm. per 100 c.c. of blood, red blood count 3.07 million, white blood count 21,900 with 87 per cent polymorphonuclear leukocytes. Urinalysis was entirely normal. Two hours later another blood count showed 20,150 white blood cells with 77 per cent polymorphonuclear leukocytes. The diagnosis at this point was "probable appendicitis."

At laparotomy the appendix was found to be quite normal, but there were approximately 400 c.c. of fresh blood in the abdominal cavity. The uterus was of about the size of a six months' pregnancy and was mottled and diffusely purple in color, but was normal in consistency. Both tubes and ovaries appeared quite normal, and there was no blood coming from the fimbriated end of either tube, nor from any of the broad ligament vessels. The abdominal incision was freely enlarged, and a very careful examination of all the abdominal and pelvic organs, including the mesenteric and omental vessels, revealed no demonstrable bleeding point to account for the hemoperitoneum. The free blood was removed from the abdominal cavity and the incision was closed. The patient was given 1,000 c.c. of whole blood and large doses of vitamin K during and after the operation. The postoperative course was uneventful and the patient was discharged, ambulatory, on the seventh postoperative day.

On Nov. 11, 1952, the patient was readmitted in active labor, and delivered of a slightly premature-looking male infant weighing 5 pounds, 13 ounces, after a labor of four hours and 15 minutes. Both the mother and child did very well, and were discharged from the hospital on the fifth postpartum day.

Summary

A case of spontaneous intra-abdominal hemorrhage in a 30-year-old pregnant multigravida is reported. The preoperative history and physical findings were strongly suggestive of acute appendicitis, which, however, was not found at laparotomy.

A review of the literature reveals this condition, "abdominal apoplexy," to be quite rare, and it is almost never diagnosed correctly prior to operation or autopsy. I have been able to find only 40 previously reported cases of spontaneous intraperitoneal hemorrhage, and there was no mention made of the coexistence of pregnancy in any of the 12 women patients included in these 40 cases.

References

1. Tanna, J. F.: Am. J. Surg. **73**: 132, 1947.
2. Sharp, W. E., Jr., and Horton, H. S.: Ann. West. Med. & Surg. **3**: 322, 1949.
3. Darling, A. P.: Surgery **27**: 911, 1950.
4. Ross, F. P.: Ann. Surg. **131**: 592, 1950.
5. Becker, W. F.: New Orleans M. & S. J. **104**: 185, 1951.
6. Hahn, G. A.: AM. J. OBST. & GYNEC. **66**: 185, 1953.

HEPATITIS IN A PREGNANT PATIENT WITH UREMIA

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(From the Obion County General Hospital)

THIS 22-year-old white woman, para 0, was admitted to the Obion County General Hospital at 2:45 P.M. on Aug. 24, 1952. The estimated date of confinement was Aug. 30, 1952. Up until ten days before admission the patient had been well, but since that time her feet had begun to swell; she had malaise; her skin had itched for five days, and for two days she had been lethargic. Blood pressure was said to have been elevated. Two days before admission she began to have abdominal pain and was nauseated. The color of the urine and feces was not noted. For two weeks before admission she had received ½ grain of phenobarbital four times a day and ammonium chloride as a treatment for toxemia. On the morning of the day of admission she began to bleed, bright red and dark red blood coming from the mouth, nose, bladder, and vagina. The urine had been scant for two days.

On admission the patient was in a coma. An icteric tint of the skin, mucous membranes, and scleras was noted. Breathing was deep, regular, and fast. Blood pressure was 158/80. The pupils reacted to light but not to accommodation. The eye grounds were normal and the neck was not stiff. No bleeding lesions could be seen in the mouth, but a small eroded area was seen in the right nasal septum. The lung fields were clear to percussion and auscultation. The heart was not enlarged, the rate was 84, the beat was regular, and no murmurs were heard. The abdomen contained an intrauterine pregnancy; the height of the fundus was 28 cm. No fetal heart tones were heard. The vertex was noted as presenting and engaged. The urinary bladder was enlarged to near the umbilicus. The liver could not be palpated. On rectal examination a soft mass was palpated which felt like a degenerating skull with bones freely movable. The cervix was 1 cm. thick and dilated 3 cm. There was pitting edema of the lower extremities extending up to the knees. Reflexes were hypoactive with almost no voluntary movement of the lower extremities.

On admission, the red blood count was 5.25 million, the hemoglobin 14 Gm. A catheter was passed and 485 c.c. of bloody urine obtained. Microscopic analysis revealed granular and fatty casts in addition to numerous red blood cells. The nonprotein nitrogen was 62, the icteric index was 58.8, blood type O, Rh positive. Anteroposterior and lateral x-rays were made of the pelvis which revealed a fetus near term lying in left occipitoanterior position with the skull bones overlapping. The pelvis was gynecoid and adequate.

A provisional diagnosis was made of toxemia of pregnancy, hepatitis, and labor with a dead fetus.

An infusion was begun of 10 per cent glucose in water intravenously, and in the course of the next six hours the patient received 150 mg. vitamin K intravenously and intramuscularly. One thousand cubic centimeters of blood was cross-matched and provision was made to give direct transfusion if necessary. No fibrinogen was available. Three hours after admission the patient was delivered of a macerated 6 pound, 8 ounce male infant by outlet forceps under pudendal block analgesia of 1 per cent procaine. There were no tears and no episiotomy was done. The initial blood loss was approximately 200 c.c. She was given 1 ampule of Ergotrate and 10 c.c. of calcium gluconate intravenously. Twenty minutes after delivery of the placenta, the uterus relaxed and hemorrhage began. Transfusion was begun immediately and continued at varying rates for the next twelve hours until she had received a total of 3,000 c.c. of blood. Eight hours after delivery the blood pressure began to drop, the

pulse became very fast and thready, and slight cyanosis occurred. Oxygen and rapid digitalization were begun. During the first twelve hours after delivery the patient vomited six times and each time the vomitus contained dark blood. The blood pressure became stable at 140/90 and the bleeding slowed to a normal amount. After the first day the patient was in a deeper coma, more icteric, and the urinary output was less than 1,000 c.c. daily with a specific gravity of 1.010. With the elevation of the nonprotein nitrogen she developed hiccoughs.

A plan of therapy was instituted whereby she would receive 300 mg. of Cortone the first day, 225 mg. the second and third days, and then 100 mg. thereafter. She would receive 1,000 c.c. of 10 per cent glucose in water plus the amount of her urinary output every day. The indwelling catheter would be opened at intervals as necessary, rather than to let the tip of the catheter furthur traumatize the bladder. Oxygen and digitalis were to be maintained until improvement began. Despite the hiccoughs sedation was withheld inasmuch as most drugs used might be toxic to the liver.

On the third postpartal day the nonprotein nitrogen reached its greatest height of 106 and the icteric index was 90. The urinary specific gravity went up from 1.010 to 1.020 and the output to 2,000 c.c. daily. From that time on there was a reversal in the findings and improvement was noted from day to day until her discharge two weeks after delivery. On the fifth day she began to respond from her coma but was not completely rational until ten days after the delivery. Upon questioning her later on, we learned that she had no memory whatsoever of anything that had happened from a week before delivery until the time of her discharge from the hospital.

At no time during her hospital stay could the liver be palpated. The stools were clay colored the first week, and the urine contained bile. The nonprotein nitrogen returned to normal limits one week after delivery but the icteric index did not become normal until six weeks after delivery. The urine continued to contain albumin and casts until shortly before discharge from the hospital. The blood pressure was 120/70 upon discharge.

After being discharged to her home she continued to receive a fat-free high-protein diet and was kept in bed for four weeks. Periodic home visits were made during this time, blood and urine specimens being collected and analyzed. Three months after delivery the uterus was still two and one-half times normal size and it was necessary to give Ergotrate to control some bleeding at that time.

Six months after delivery urine, complete blood count, cephalin flocculation, and Bromsulphalein tests were normal.

One year after delivery the patient was still normal.

The symptoms and findings presented by this patient were considerably more severe than ordinarily seen in a patient with hepatitis. Inasmuch as there is ordinarily some enlargement of the liver in hepatitis, and there was none demonstrated in this patient, it was suspected that she actually had acute yellow atrophy of the liver. However, no biopsy was performed and this could not be proved. It is thought that the use of Cortone proved a valuable adjunct in the treatment of this condition and was perhaps responsible for the survival.

A SIMPLIFIED OBSTETRICAL PHANTOM

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EARLY in 1949, while casting about to gather teaching material for courses in which the United Nations Children's Fund (UNICEF) was helping the Chinese to prepare students for rural midwifery, Dr. Kati Lim, Professor of Obstetrics at Pei Ta Medical College, Peking, was kind enough to lend us an obstetrical phantom of the kind described by Dougal[1] of Manchester.

The phantom consists of a plain rectangular block of glazed porcelain earthenware in which the inner aspect of the pelvis is accurately modeled, so that a fetal doll can be made to pass through the porcelain birth canal and the progress of labor demonstrated. The outer surfaces are plain and flat and, unlike those of many fancy manikins, they make no pretense of imitating the female form. Plainness, far from detracting from the manikin's usefulness, enhances it, for it focuses attention on the pelvic canal.

We added some details that proved useful. A Chinese carpenter did an excellent job in copying the Dougal phantom and making the modified model in wood. Wooden cylinders representing thighs were attached to the corners of the block by dowels; they could readily be pulled off and removed when not needed. They were used to teach students how to drape a woman in labor; the cylinders were necessary, for sheets slid off the smooth porcelain block. We also screwed onto the pelvic outlet a metal ring in which a sheet of rubber cut from the inner tube of an automobile tire was spanned. With a slit cut into the middle of the sheet of rubber, these external genitals offered about the right resistance to delivery of the fetal doll. The phantom, as Dougal said, was simple and easily kept clean. It was also exceedingly cheap; including the doll it cost less than five dollars. It was heavy and not easy to move, but this was no drawback as long as classes were conducted in a fixed classroom; indeed, the heavy, solid phantom made manipulation of the doll more secure.

Later, working at the New York headquarters of the Children's Fund, somewhat different requirements arose. In some countries, such as India and Pakistan, instructors travel about from village to village, giving classes to small groups of country midwives. To carry so heavy a porcelain block about with them would be impossible. Furthermore, not more than four or five students, closely grouped around the instructor, can see what is going on in an opaque phantom during demonstration of the process of delivery. It was thought that larger groups might be able to watch were the model transparent. The transparent manikin described in this Journal by Wakerlin and Whitacre[2] has solved part of these difficulties. However, during our inquiries what seemed a simpler solution finally came to mind, that is, to omit the superfluous exterior of the phantom altogether and reproduce only the essential part to which the student needs pay attention—the abdominal cavity and the birth canal.

In the summer of 1952 we were fortunate in receiving a communication from Dr. George Blaine, of the Anatomy Department of the University College of the West Indies, Jamaica,* and with his help and collaboration evolved a model of a transparent plastic

*Among other help, Dr. Blaine has used the services of handicapped Jamaicans in producing the model; thus we hope that it may be useful in more ways than one. Those interested in procuring the phantom and a carrying case may communicate with Dr. George Blaine, Department of Anatomy, University College of the West Indies, Mona, St. Andrews, Jamaica, B.W.I.

pelvic canal and abdominal cavity to which two transparent thigh pieces and rubber external genitals are joined. A photograph supplied by Dr. Blaine explains the model better than words (Fig. 1).

Outlines of the bony structure surrounding the birth canal and the abdominal cavity are marked on the plastic. The phantom is securely fastened to a wooden base which can be screwed, bolted, or clamped firmly to a demonstration table. A removable rubber sheet, edged with a number of metal eyelets, buttons over lugs at the side of the base; when spanned across the abdomen, the sheet permits the student to palpate the position of the fetal doll while fellow students look through uncovered portions of the model and check the diagnosis. In demonstrating the process of labor a group of about ten students can follow the movement of the doll through the transparent pelvic canal.

Fig. 1.—Transparent phantom viewed from lower end.

The phantom is light and compact. It weighs 8½ pounds; a traveling midwife-instructor can easily carry it by hand in a case the size of a small suitcase. It is inexpensive; it costs, with the fetal doll, about one-fifth of the price of most manikins, an important detail for governments with health budgets totaling less than one dollar per annum per head of population.

References

1. Dougal, Daniel: J. Obst. & Gynaec. Brit. Emp. 40: 99, 1933.
2. Wakerlin, R. C., and Whitacre, F. E.: Am. J. Obst. & Gynec. 64: 1378, 1952.

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Review of New Books*

Atlas of Exfoliative Cytology. By George N. Papanicolaou, M.D., Ph.D. 176 pages with 84 illustrations. Cambridge, Mass., 1954, Harvard University Press. $18.00.

The increase in the knowledge of exfoliative cytology has to a large degree been due to the investigations of Dr. Papanicolaou and therefore appearance of a new book by him is greeted with enthusiasm.

This latest book is published in a unique style. It is a looseleaf manuscript with large rings so the pages do not bind and consequently have little tendency to tear. This method of publication allows for additions in the future. The softness of the binder, however, is not conducive to wear and tear. This may be an objection if the book is used frequently without due care.

Exfoliative cytology has been most frequently applied to the study of the female genital tract but other body fluids are amenable to this method of study. This book deals with most of such fluids, including the methods of obtaining them and the techniques of fixing and staining. The study of the cytology of the systems of the body other than the female genital tract is in its infancy and Dr. Papanicolaou rightly emphasizes that much has to be learned.

The colored plates are excellent and their descriptions although brief are adequate. Because of the looseleaf arrangement, one is able to remove a plate and compare it easily with any other plate or description.

It appears from the text that many abnormal cells which previously had been interpreted as suspicious of malignancy now are considered abnormal but not necessarily indicative of malignancy. This is in keeping with the thought of most workers in this field. Inflammatory processes frequently produce bizarre cells that can be misinterpreted by the inexperienced person.

One aspect of exfoliative cytology of the female genital tract is not included and yet may be most important, namely, the vaginal cytology of the prepubertal girl in health and disease. Cytology at that time of life may be very useful in the diagnosis of endocrine disturbances and it is regretted that this has not been included.

This latest work of Dr. Papanicolaou is very worth while and should find a wide demand. It can be highly recommended, especially as a reference book.

Chronic Iliac Pain in Women. By H. B. Atlee, M.D. 65 pages with 6 illustrations. Springfield, Ill., 1954, Charles C Thomas. $2.50.

This book is a short, easily read monograph summarizing the main causes of chronic iliac pain. The book is divided into nine sections in which different disorders, such as chronic appendicitis and painful ovary are described briefly. The book, while describing a serious problem, is written in a humorous vein. For example, in describing the so-called "cecal syndrome"—"Some people feel that if their bowels do not move today, the atom

*The Advisory Committee on Policy has agreed that most book reviews need not be signed.

bomb will fall tomorrow, and harassed by this fear, they do everything to whip their poor bowels into action every morning except to relax on the toilet seat long enough to give them a chance to empty themselves on their own."

The main premise of the book is that surgery should be performed for chronic iliac pain only if a definite diagnosis is made. Otherwise patients will be subjected to needless surgery, and still retain their pain. Because of the message it carries, young gynecologists and general surgeons would do well to read this book.

Les Groupes sanguins chez l'homme. Étude sérologique et génetique. By Jacques Ruffie, Assistant Professor, Legal and Occupational Medicine, University of Toulouse. 212 pages. Paris, 1953, Masson & Cie. 1.200 fr.

The universal practice of blood transfusion, the problems of fetomaternal immunization, and a variety of medicolegal questions, make the subjects of blood groups one of great practical and theoretical importance. Dr. Ruffie's book is a detailed account of the basic information available on this vast subject.

The four major blood groups, the Rhesus, Lewis, MNSs, PQ, and seven other minor systems are examined, and the genetic aspects, statistical analysis, and clinical importance of each are thoroughly discussed.

A general introductory chapter on immunization phenomena of the blood is outstandingly clear and will be of value to anybody who is not particularly well acquainted with these matters. The book contains a discussion of "some elementary principles of the statistics of probability" which is not at all elementary but will help the reader to understand the statistical analysis of each system.

When a fundamental problem is discussed, the author gives an ample résumé of the major theories involved, such as those of Hirszfeld, Morgan and Watkins, Boorman, Dodd, and Gilbey, on the H antigen.

The bibliography is extensive and up to date.

The reader will not find here any original contribution, but he will benefit from the clarity with which the subject is treated.

Lehrbuch der Geburtshilfe. Edited by Prof. Dr. Th. Koller, Basel, Prof. Dr. E. Held, Zurich, and Prof. Dr. W. Neuweiler, Bern, Switzerland. Second edition. 851 pages with 348 illustrations. Basel, 1953, S. Karger Verlag. Swiss francs 62.40.

This volume constitutes the second part of a three-volume text on obstetrics and gynecology. Consequently, it does not embody any description of obstetrical procedures, which are reserved to the third volume.

The book is very well arranged. It contains sections on embryology, normal pregnancy, normal delivery and puerperium, the physiology of the newborn, multiple pregnancy, the pathology of pregnancy, extrauterine gestation, abnormal delivery, complications of the puerperium, monstrosities, and the pathology of the newborn.

Each of the different sections has been written by an authority in his field. Altogether, this constitutes a most impressive textbook. The sections on monstrosities and fetal pathology are especially good. These subjects are much more fully covered than is customary in obstetric texts.

Roentgen pelvimetry receives scant consideration. The classification of contracted pelvis is based upon etiological factors, rather than morphology. A low-protein diet is advocated in toxemia. Curettage is not performed in incomplete abortion unless all other measures have failed. One of the illustrations in the section on infant resuscitation shows jackknifing of the infant as a means of artificial respiration. With these, as well as some other features, the reviewer would take issue.

However, with due allowance for differences in opinion, this remains a thorough and scholarly survey of the field of obstetrics. It may be highly recommended.

Handbook of Gynaecological Diagnosis. By Walter Neuweiler, M.D., Professor of Midwifery and Gynaecology and Director of the Gynaecological and Obstetrical Clinic in the University of Berne. 448 pages with 406 illustrations. New York, 1952, Grune & Stratton. $12.00.

As stated in the author's preface, this book is merely a supplement to the many recognized textbooks in gynecology. If the reader will bear this in mind, he will find it of extreme interest. The methods of obtaining a complete gynecological history are aptly explained. They are further enhanced by a careful consideration of such things as constitutional types and symptom complexes. The techniques of performing and interpreting various gynecological examinations are lucidly portrayed and described. The section on hysterosalpingography is especially well illustrated.

Although the importance of colposcopy in the diagnosis of cervical malignancies is stressed, it is unfortunate that little mention is made of the value or significance of the Papanicolaou smear. Furthermore, in the description and illustration of the lymphatic spread of cervical carcinoma, there is no inclusion of the obturator lymph nodes. In view of the accepted practice of early ambulation in clinics in this country it is interesting to read the author's statement that following a uterine curettage the patient "needs at least two to three days' rest in bed."

The author is to be commended for the careful organization of his material and the excellent illustrations. Just as previous texts on differential diagnosis in other branches of medicine have been of value, the *Handbook of Gynaecological Diagnosis* should be a useful guide not only to the medical student but also to the practicing physician in the field of gynecology.

Die Kreuzschmerzen der Frau, Ihre Deutung und Behandlung gynaekologische Orthopaedie. By Dr. Heinrich Martius, Göttingen, Germany. Fourth Improved Edition. 166 pages with 73 black and white illustrations. Stuttgart, 1953, Georg Thieme. DM 19.50.

This book covers the twilight zone between gynecology and orthopedics in the very difficult field of low back pain. It is divided into two sections. The first deals with low back pain in women, caused by diseases of the viscera of the true pelvis. The second, and larger portion, concerns itself with low back pain due to changes in the skeleton, the local musculature, and even such culturally determined factors as high heels.

The author emphasizes the importance of accurate etiological diagnosis preceding therapeutic intervention and the pitfalls of attempting treatment without adequate diagnosis. Both diagnostic and therapeutic procedures are explained. It is pointed out that the erect posture of man and easy childbirth are opposed to each other and that the skeleton of the human female represents a balance between the two which is easily upset.

This volume covers very adequately a field which is of constant interest to the gynecologist and it is well worth his attention.

The Nursing Mother. By Frank H. Richardson, M.D. 204 pages. New York, 1953, Prentice-Hall, Inc. $2.95.

This small volume is written primarily for the pregnant woman. Although it cannot be denied that breast feeding is to be preferred to bottle feeding, the woman who does not breast feed her infant for any reason should not be condemned to the point where marked psychological disturbance is produced. This book might well cause this undesired result even though the author occasionally attempts to prevent it.

The section devoted to proving that the breast is better than the bottle for feeding infants is not grounded on very good scientific evidence. Infant death rates of one era should not be compared with those of another era unless all factors, not just one such as breast feeding, are considered. The evidence presented is from work done twenty-five to thirty years ago. Inquiry by the reviewer of leading authorities in the field of pediatrics disclosed there are no current authoritative studies that show any difference between the infant mortality rates of bottle-fed and breast-fed infants. There is a higher incidence

of gastrointestinal disturbances in the second six months of life in the bottle-fed group. The statement that facial development is better in the breast-fed infant than in the bottle-fed infant will be received with skepticism.

The author pictures the bottle-fed baby as disregarded by his mother, fed by a stranger in strange surroundings, and doomed to permanent psychiatric aberrations. This is by no means a usual occurrence and should provoke some righteous indignation.

There are many places in the book where scientific logic is not sound. It is stated that therapeutic abortion is done to save the life of a woman, but then the author states, "Such an interference with nature is attended with more danger than would have been risked had the woman gone on to a full-term delivery."

Several quotations are given but rarely is the name of the author of the quotation mentioned. Not only is this poor taste, but it also deprives the reader of the authority for the quotation.

It is unfortunate that in a book of this type so much emphasis is placed on "natural childbirth," for this might tend to disrupt the relationship between patient and obstetrician if the latter is not an enthusiast for this form of labor.

A book of this type is needed in American medical literature to point out the advantages of breast feeding but the criticisms mentioned illustrate weaknesses which may limit its usefulness.

La Sterilita nel maschio. By Guglielmo Longo. 520 pages with 87 illustrations. Naples, 1953, Diffusion Scientifique Internationale.

By far the greatest part (eight-tenths) of the work is dedicated to the normal anatomy and physiology of the male genital system and to a classification of the various forms of sterility.

There is a very exhaustive chapter on clinical and laboratory techniques which includes all the tests more commonly used in the United States and many tests which are rarely used.

Therapy is dealt with in one and the smallest chapter, and it is subdivided into:

A. Treatment of the deficiencies of coitus; these may be treated according to the etiology of the specific case, by (1) hormones, (2) electroshock, electrical cauterization of the nasal mucosa, (3) infiltration of the hypogastric ganglion and similar procedures, (4) psychotherapy (but psychoanalysis is considered "not useful").

B. Treatment of obstructions of the seminal tract; these demand surgical treatment.

C. Treatment of the disturbances of spermatogenesis; hypogonadism (deficiency of both the endocrine and the spermatogenic functions) may respond to treatment with gonadotropin. The ability of testosterone to increase spermatogenesis is open to debate; it has a more definite effect in re-establishing the motility of spermatozoa.

Dr. Longo's work is essentially a recapitulation of the basic known facts about male sterility. While there is no original contribution to the understanding of the causes, nor any statistical observation sufficiently large to attract attention, the available material has been examined thoroughly and is clearly presented.

Annual Report on the Results of Treatment in Carcinoma of the Uterus, vol. 8. Edited by James Heyman, Stockholm, Sweden. 247 pages. Stockholm, 1953, Norstedt & Son.

This is the eighth volume of a valuable publication issued approximately annually, and sponsored by The American Cancer Society, The British Empire Campaign, and other prominent institutions concerned with the cancer problem. The editor of the series is Dr. James Heyman of Stockholm, and the plan of each volume is to summarize reports treatment of carcinoma of the female genital tract. Previously, carcinoma of the cervix from leading institutions throughout the western world on the subject of the results of has been the only female genital cancer specifically reported, and irradiation has been the only method of therapy considered. The scope has finally been extended in the present report to include carcinoma of the endometrium, and apparently the intention of the future editions is to include summaries dealing with ovarian carcinoma.

The statistics presented in this volume were collected from 69 different institutions, 13 of which are located in this country. Fifteen different countries are represented. The results cover a total of 83,291 cases of uterine carcinoma. There are carefully prepared preliminary essays on such topics as the desirability of improved facilities for obtaining reliable therapeutic statistics, rules for collaborators when reporting on cases of non-invasive carcinoma, special problems relating to statements on carcinoma of the fundus, and a careful statement of staging criteria. The editorial committee has been commendably zealous in attempting to attain the ideal of absolutely uniform criteria for clinical classification of cases of genital cancer to permit comparative evaluation of statistics. The present edition contains a praiseworthy attempt to reach uniformity of interpretation of the well-known bullous edema of the vesical trigone mucosa. The committee states that this should not be considered as a sign of carcinomatous involvement of the bladder unless there are other signs of involvement such as fistula, ulceration, carcinomatous nodules, or other lesion from which a confirmatory biopsy can be obtained. Obviously, this publication must be in the reference file of all departments treating patients with female genital carcinoma.

Hormonal Control of the Pelvic Girdle and Sexual Endocrinology. By Maurice Marois. 176 pages with 12 plates. Paris, 1953, Masson & Cie. $2.55.

An elaborate and comprehensive monograph covering all aspects of the problem of the hypothetical hormone, relaxin, which is postulated to be responsible for pelvic relaxation in various species has been written by the codirector of the Laboratory of Experimental Morphology and Endocrinology of the College of France. The starting point of this elaborate book is an examination of Hisaw's hypothesis that symphyseal separation in the guinea pig is due to an unidentified hormone, relaxin. Professor Courrier, director of the Laboratory of Experimental Morphology and Endocrinology at the College of France, has believed for some time that relaxin is not a specific substance, since it is possible to produce separation of the pubic bones in a castrated female guinea pig by means of combined administration of follicular hormone and of progesterone. This hormone combination is not effective when the uterus is absent; and the idea that there is a specific uterine hormone is raised. This monograph attempts to review very comprehensively all the literature on the subject, and to report the results of Marois' own investigations.

After performing extensive experimental studies in the guinea pig, the author has reached several interesting conclusions. He was able to confirm that the use of estradiol and progesterone as mutual synergists produces symphysal separation only when some uterine tissue is left in the animal. Only a small amount of uterine tissue is necessary for the mediation of this effect. If hysterectomy is performed in animals who have appreciable symphyseal separation, symphyseal closure is produced, without reference to the doses of estradiol and progesterone administered after the procedure. The author believes that the uterus acts as an intermediate organ permitting mutual interplay between progesterone and symphyseal ligamentary structures. The hypotheses that he considers are, first, that the uterus is capable of transforming progesterone from a potentially to an actually functioning substance with respect to pelvic-girdle relaxation; or, second, that progesterone is capable of stimulating the uterus to produce the hypothetical uterine hormone.

On the basis of these preliminary observations, Marois turned his attention to the reactions of the uterus to various combinations of sex hormones. His work suggests modification of the classic observations concerning the effects of estrogen or of progesterone alone on the endometrium. Marois performed careful studies on the effects of massive doses of estradiol on the guinea pig uterus, and observed hyperemia and edema followed by necrosis and eventual scar formation of the uterus; this could be carried experimentally to the point of replacement of the entire endometrium and of much of the myometrium by dense scar tissue constituting, in effect, a hormonal hysterectomy. Such animals behaved exactly as experimentally hysterectomized animals.

A great many pages of the monograph are devoted to the tentative exploration of several avenues of approach to the identification of a specific hormone capable of producing symphyseal ligamentary relaxation in the guinea pig. Marois is frank to admit that he has not been able to solve this problem satisfactorily. He has confirmed previous observations that extracts of corpus luteum are capable of producing pubic symphyseal relaxation in the female guinea pig very much more readily than the synergistic action of follicular hormones and progesterone. But the confirmation of the well-known fact that symphyseal relaxation may be produced in these various ways has not been established beyond reasonable doubt, since this would involve the isolation and purification of whatever specific agent is responsible for these hormonal interactions. The major obstacle remains the lack of reliable, critical biologic tests for assaying the activity of tissue extracts.

In summary, this massive monograph, virtually encyclopedic in approach, broadly speculative and imaginatively presented, represents a stocktaking of the present state of our ignorance on this much debated subject. In Marois' own words: "In spite of the extent of the data already acquired, we are left with more darkness than light. It is hoped that this work will constitute an invitation to further research." Only an elementary knowledge of French syntax is necessary for the reading of Marois' elegantly clear style, a model of its kind. The carefully compiled bibliography makes the monograph an essential item for the library of all investigators of these problems.

Le Pneumopatic sufethine del feto e del neonato. By Guiseppe Valle. 209 pages with 54 illustrations. Torino, Italy, 1953, Minerva Medica.

Dr. Valle is the director of the Clinic of Obstetrics and Gynecology at the University of Perugia in Italy. In this book he presents an extensive review of the literature relating to pneumonic infections in the fetus and the newborn. In a careful, organized, and scholarly manner he correlates all of this material with his own observations and researches. There is a complete and exhaustive bibliography.

The book is arranged in ten chapters: The first chapter is a historical introduction of the subject. The second chapter deals with classification of the pneumopathias. He proposes his own scheme which divides the subject into three main periods: prenatal, intranatal, and neonatal. These are further broken down into smaller subdivisions with regard to the causative agents involved.

Subsequent chapters deal chiefly with etiology and pathogenesis. There is an interesting discussion as to the routes infection may take to cause pneumopathia in the fetus, and these are clearly illustrated with diagrams and sketch drawings. Many charts are presented reviewing the organisms involved and the problem of placental transmission.

The importance of the aspiration of amniotic fluid by the fetus upon birth, is emphasized, particularly if the membranes were prematurely ruptured and the amniotic fluid infected.

The book offers no unusual new theories or solutions. It does, however, serve several important functions. First, it is a good review of the subject matter; second, it suggests several good research problems; third, it alerts the obstetrician to the fact that he is always dealing with two patients, mother and fetus, and that he is responsible for the course and welfare of both; and last, it urges the pediatrician to be more cognizant of the pre-, intra-, and neonatal periods of the infant, so that ultimately his attention may be more effective.

Seventy-Five Years of Medical Progress, 1878-1953. Edited by Louis H. Bauer, M.D. 286 pages. Philadelphia, 1954, Lea & Febiger. $4.00.

This enlightening book followed the First Western Hemisphere Conference of The World Medical Association, which was held in Richmond, Virginia, in April, 1953. The object of this conference was to recall the medical progress which has been attained during

the past seventy-five years. The papers were contributed by our most distinguished colleagues in the field of medicine and in the different medical specialties.

Each author has endeavored to give a brief review of the history and the distinctive events in his field and to appraise these achievements. It is interesting to obtain this retrospective view of how the various specialties have developed and have become defined. The present extent of our knowledge is also reviewed. The text has not neglected the field of general practice, its role in past progress, and the importance of the general practitioner as a central figure in the care of patients.

The book is refreshing as it makes the reader cognizant of the primitive status of medical practice which existed seventy-five years ago. It is thus that we realize that the time, effort, and cost of our present medical organization are well worth while.

Pelvic Relaxations and Herniations. By James Wilson, M.D. 64 pages with 35 illustrations. Springfield, Ill., 1954, Charles C Thomas. $2.75.

In this monograph for the American Lecture Series, the author points out that the work is designed for students.

It first covers the clinical anatomy of the normal female pelvis and then goes on to outline the most important of the pelvic fascial relaxations and herniations. The etiology of each is considered from an anatomical and physiological viewpoint. No attempt is made to explain in detail the technique of operative procedures but rather the general principles employed are discussed. Adequate reference to the standard operative procedures for each condition is given at the end of each chapter.

The work is supplemented with excellent diagrams and drawings which assist in a more complete comprehension of the text.

The monograph is concise and complete in its coverage of the pelvic fascial planes and their pathology.

Rh-Hr Blood Types. Applications in Clinical and Legal Medicine and Anthropology. By Alexander S. Wiener, M.D. 763 pages. New York, 1954, Grune & Stratton. $11.50.

An Rh-Hr Syllabus. The Types and Their Applications. By Alexander S. Wiener, M.D. 82 pages with 8 illustrations. New York, 1954, Grune & Stratton. $3.75.

Dr. Alexander Wiener, who has long been known as an authority on immunology, particularly in the field of isoimmunization, has written two books on the subject of Rh-Hr blood types.

The first is a large compilation of some of the author's most representative and important contributions to the subject. This serves the purpose of placing these documents in one volume with an adequate index of both subject and author. For reasons not clearly discernible the author's total bibliography is also appended. Such a collection of reprints contains much valuable material. All of this is readily available in any good medical library, however, and unfortunately, when conglutinated in this manner, the bias and, at times, uncertain temper of the author are only emphasized rather than tempered with the sound and solid contemplation and revision and revaluation so necessary to fine scientific book writing. It is thus that there is a perpetuation of certain ideas which might be proper for scientific articles of the moment but which on second thought, to say the least, do not come under the heading of proved fact. In such categories are the author's concept of the dual valence of antibodies, his diagrams of the cogwheel characteristics of antibody-antigen reaction, and his theories of the difference in antibody size as a basis for differential rates of diffusion. It is hard to say that these theoretical ideas are untrue, but it can be said that they do not represent the summation of current knowledge on the subject. Without meaning in any way to take sides, this reviewer feels that the support of the author's Rh-Hr nomenclature and the ridiculing of the Fischer-Race C. D. E. system is carried beyond the accepted bounds of scientific propriety. The latter far more easily expresses the genotype and furthermore it represents a particular type of logical reasoning which was able to forecast the discovery of the Hr_0 and Hr″ antibodies before the fact. For such reasons alone, due credit should be given.

The second volume is a small outline of 82 pages containing a brief but accurate abstraction of much of what is contained in the first volume. Although the errors and bias are still apparent, this volume makes good reading and, if absorbed, will give the reader an intelligent background for further investigation.

The articles in the first volume have been reproduced in a format similar to the ones in which they appeared. This not only makes for variation in form throughout but in some instances because of the reduction in page size makes for unnecessarily and nearly unreadable type. The paper of this volume is poor. The type and format of the second volume, in contrast, are good throughout.

In summary, it is difficult to commend the first of these two works. The Rh problem, as such, has been overemphasized because of its clinical significance. In reality it differs neither in complexity nor in concept from the entire problem of erythrocyte antigenicity. On this a broad text soundly and judiciously conceived would have been more to the point.

Obstetrical Pathology. By Dr. Jose Botella Llusia. 699 pages with 434 illustrations. Madrid, 1953, Cientrifico-Medica.

Dr. Jose Botella Llusia is Professor of Obstetrics and Gynecology at the University of Medicine in Madrid. He has written and published four books, which comprise his complete course in the elements of obstetrics and gynecology, of which this title is one. The other three books are entitled *Female Physiology, Obstetrics,* and *Diseases of the Female Genital Tract.*

The book is divided into three main parts: the pathology of pregnancy, the pathology of parturition, and the pathology of the puerperium. These are further subdivided into 40 chapters, which cover comprehensively all the subjects of pathological significance relating to the subject of obstetrics. The book is unique in that it is a well-organized and convenient text dealing only with obstetrical pathology.

Most of the subjects are dealt with at great length and in great detail. The 434 illustrations consist of diagrammatic sketches, photographs, and color photomicrographs. In general, the author's theories and teachings are in agreement with the universally accepted ones.

In discussing the toxemias, the author rejects the classification of pre-eclampsia and eclampsia as two separate diseases. He firmly believes they are one and the same, varying only in intensity and severity. He remarks on the apparent declining incidence of the disease in Spain, and relates this to better prenatal care and better nutrition. His preferred plan of treatment is as follows: morphine sedation, inhalation of 5 per cent oxygen with 20 per cent carbon dioxide, administration of hypertonic glucose and intramuscular magnesium sulfate.

The author's comprehensive discussion of all the complications of pregnancy includes, besides the usually discussed ones, various liver dysfunctions, cholecystitis and cholelithiasis, appendicitis, mouth lesions, hernias, dyspepia, peptic ulcers, and intestinal colic. Many of Dr. Llusia's statements are quite positive, indeed interesting, although there is a definite lack of reference support. For instance, he says that gastric ulcer is rare in pregnant patients for three reasons: (1) there is less gastric acidity; (2) elevation of the stomach by the pregnant uterus lessens its distention and better vascular circulation results; (3) the increased estrogen enhances better healing of the gastric mucosa.

The subject of cardiac complications is dealt with extensively. It is his opinion that repeated pregnancies in a cardiac patient, if well handled, do not affect deleteriously the cardiac status, general health, and longevity of the patient.

The subject of abortion is thoroughly discussed along with the problem of criminal abortion. The author speculates that there are 50,000 criminal abortions performed annually in Spain. In the Madrid Maternity Hospital there were 18,000 babies born in the years from 1939 to 1949, and 4,800 abortions. The author assumes that 10 per cent of all births should result in spontaneous abortion and that the remainder would be criminally induced. The mortality rate for abortions in this period was 3.6 per cent.

The subject of dystocia is particularly well organized and completely covered.

The book has no bibliography. The lack of bibliography and references and the areas of loose reasoning and invalid assumptions detract from the total value of the book. This remains, however, a good, convenient, well-organized textbook to orient and instruct medical students with the subject of abnormal obstetrics.

Books Received

The following books have been received and selected reviews will appear in later issues.

TITLE	AUTHOR	PUBLISHER
el Cancer Ginecologico	Juan Carlos Ahumada y Colaboradores	El Ateneo, Buenos Aires
The Digestive Tract in Roentgenology Second edition	Jacob Buckstein	J. B. Lippincott Co., Philadelphia. $30.00
Grundlagen und Ergebenisse der Sulfonamidanwendung gegen Karzinomstreptokokken	Klaus Niedner	Georg Thieme, Leipzig. DM 21
The Hypertensive Disorders of Pregnancy	Ernest Page	Charles C Thomas, Springfield, Ill. $3.75
Resuscitation of the Newborn	Joseph Russ	Charles C Thomas, Springfield, Ill. $2.50
Cancer of the Female Genital Tract	Herbert F. Traut and Ralph C. Benson	Davis, Delaney, Inc., New York
Erythroblastosis Fetalis, Report of the Seventh M & R Pediatric Research Conference	Charles Janeway, Chairman	M & R Laboratories, Columbus, Ohio
Menorrhalgia-Menstrual Distress	William Bickers	Charles C Thomas, Springfield, Ill. $2.75
Proceedings of the Society for the Study of Fertility Number V, 1953		W. Heffer & Sons, Ltd., Cambridge, England
The Intimate Problems of Women	Henry B. Safford	Hawthorne Books, Inc., New York. $3.95
Die Variationsmoglichkeiten im Aufbau der Uterusschleimhaut in den einzelnen Phasen des Mensuellen	Heinz Behrens	Georg Thieme. DM 9.60
A la Recherche d'une éthique médicale	Louis Portes	Masson & Cie, Paris. 800 fr.
Die Viruskrankheiten in der Gynäkologie und Geburtshilfe	Meta Sander	Georg Thieme

In Memoriam

ARTHUR K. KOFF, born in 1905, died suddenly on June 28, 1954. He had been Chairman of the Department of Obstetrics and Gynecology at Michael Reese Hospital since Jan. 1, 1951, and was also on the Associate Staff of the Chicago Lying-in Hospital of the University of Chicago.

Correspondence

Vitamin E for Vulvovaginitis

To the Editors:

It is a little difficult to write about vitamin E for vulvovaginitis or diabetes and omit mention of our priorities in both fields, but I notice that Dr. Ant has managed it in the March, 1954, JOURNAL.

Butturini first suggested that alpha tocopherol was useful in diabetes mellitus in 1945, but his work was unknown on this continent when we reported the same observation independently in 1947. Our interest in the subject really had dated from 1936. There have been confirmations of this suggestion by a number of workers since, Block especially having stressed its value for diabetic complications.

In 1936 and 1937 I first mentioned that alpha tocopherol was uniquely valuable for the treatment of vulvovaginitis, especially at the menopause. Since that time I have used it extensively, summarizing some of my data in 1950 in a journal which Dr. Ant receives. In this last article there is specific mention of the successful use of alpha tocopherol in diabetic vulvitis.

May I add that in a day when it is widely recognized that insulin and diet control the hyperglycaemia of diabetes mellitus, but do little for the other important aspect of the disease, progressive general vascular degeneration, alpha tocopherol plugs the leak in the therapeutic boat. No diabetic can now be treated adequately unless he is given vitamin E, as Butturini makes abundantly clear in our book on the subject just published.

Yours very truly,

EVAN V. SHUTE, M.B., F.R.C.S.(C)

THE SHUTE INSTITUTE FOR CLINICAL
AND LABORATORY MEDICINE
LONDON, ONTARIO

MARCH 1, 1954

References

Shute, E. V.: Canad. M. A. J. **37**: 350, 1937.
Shute, E. V.: J. A. M. A. **110**: 889, 1938.
Shute, E. V.: J. Obst. & Gynaec. Brit. Emp. **49**: 482, 1942.
Shute, E. V.: Summary **2**: 34, 1950.

Treatment of Patient With Postabortal Clostridium Welchii Infection

To the Editors:

I have read the article, "Spherocytosis as a Manifestation of Postabortal Clostridium Welchii Infections," by Drs. G. G. Hadley and R. D. Ekroth, in the March, 1954, issue of the JOURNAL. I was much surprised to read that they did a hysterectomy on such a severely ill patient as Case 1. I see no reason for the hysterectomy. In fact, to my way of thinking, it would certainly be contraindicated. What were their indications for the hysterectomy? To me, the treatment of this patient would have been blood transfusions, antibiotics, and polyvalent antiserum.

HOWARD C. DUCKETT, M.D.

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APRIL 2, 1954.

Changing Trend in Treatment of Cervicitis

To the Editors:

Eleven years ago I reported in this JOURNAL (Vol. 46: page 400, September, 1943) on "The Local Use of Acid Media and Sulfa Drugs in the Management of Cervicitis and Vaginitis." In September of last year an outline of therapy for benign lesions of the cervix was presented at the Mississippi Valley Medical Society meeting in Springfield, Illinois. A review of the work done in the Washington University Cervicitis Clinic in the Out-Patient Dispensary is now in progress of reporting and will be presented some time next year.

The changing trend in treatment and emphasis in the management of cervicitis has been noted and becomes the subject of this letter.

There is a marked reduction in the number of conizations of the cervix uteri performed both in the outpatient clinic and in private practice. There are good reasons for the decrease in number of conizations:

1. The control of cervical infections, first by sulfonamides and later by antibiotics. With the use of penicillin, streptomycin, Terramycin, Achromycin, etc., fewer cases of cervicitis are seen. The gonococcus is so rarely seen in the outpatient clinic today that many medical students have never seen this form of acute cervical infection and fail to recognize the condition when the unusual case presents itself.

2. The control of cervical erosion by the local use of acid media in the form of sugar (beta lactose), buffered acid jellies, and acid douches, and the prohibition of alkaline douches, which reduce the incidence of erosion of the cervix.

3. The better understanding of the concentric erosion as being physiological under most conditions and requiring no therapy. These erosions are reversible.

4. The better knowledge of the type of cervical lesion associated with, or a precursor of, carcinoma in situ. These lesions have been identified by the use of (1) Papanicolaou stain smears; (2) endocervical scraping; and (3) multiple punch biopsies of the cervix.

When such a condition has been well established as nonreversible, the accepted therapy is complete hysterectomy with removal of the cervix and adjacent vaginal vault cuff rather than conization of the cervix.

5. The use of Papanicolaou smears with multiple biopsies of the cervix to establish a diagnosis of cancer of the cervix rather than the examination of cervical tissue removed by conization to make a diagnosis of malignancy.

In addition to these five good reasons for limiting the use of conization, we hope that better obstetrics is now being practiced. Fewer inductions of labor mean fewer damaged cervices.

The immediate repair of childbirth laceration of the cervix in the delivery room is now a common practice. This lessens the use of questionable chemical and thermal cauterization of the postpartum cervix as an office procedure. Without doubt epithelial damage was produced by these cauterizations and later on conizations were done to remedy the lesion.

Let us keep up the good work and cut down on the number of conization operations performed on the cervix uteri.

MELVIN A. ROBLEE, M.D.

101 SOUTH MERAMEC
CLAYTON 5, MO.
MAY 9, 1954

Items

American Board of Obstetrics and Gynecology, Inc.

Applications for certification for the 1955 Part I Examinations are now being accepted. Candidates are urged to make such application as soon as possible.

All candidates for admission to the Examinations are required to submit with their application a plain typewritten list of all patients admitted to the hospitals where they practice, for the year preceding their application or the year prior to their request for reopening of their application, with the diagnosis, pathological diagnosis, nature of treatment, and end result.

Application for examination or re-examination, as well as requests for resubmission of case abstracts, must be made to the Secretary prior to Oct. 1, 1954.

Under a change of requirements for the Part I Examination, candidates must submit 20 case abstracts rather than 25 as formerly. Five of these may be from one's residency service.

ROBERT L. FAULKNER, M.D., Secretary
2105 Adelbert Road
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The following candidates were certified by the American Board of Obstetrics and Gynecology, May 17, 1945, at The Edgewater Beach Hotel, Chicago, Illinois:

Abraham, Leo Maas	1716 Myrtle	Baton Rouge, La.
Abrams, Bernard S.	10333 Carnegie Ave.	Cleveland, Ohio
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Alexander, Clarence H., Jr.	1820 Gilpin St.	Denver, Colo.
Allen, Thomas E.	210 Craft Ave.	Pittsburgh, Pa.
Allgood, Jackson L., Jr.	423 St. James Bldg.	Jacksonville, Fla.
Alsop, Webb S., Jr.	411 Nichols Rd.	Kansas City, Mo.
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Burns, William T.	902 N. Third St.	Harrisburg, Pa.
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Horowitz, Albert W.	160 Marlborough Rd.	Brooklyn, N. Y.
Houk, Preston S.	205 N. Main St.	Bloomington, Ill.
Hubbard, John F.	213 S. 17th St.	Mattoon, Ill.
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Hutto, Herman A.	4500 Olive	St. Louis, Mo.
Igel, Leo	4803 15th Ave.	Brooklyn, N. Y.
Iguina-Jimenez, Manuel A.	6 Saldana St.	Rio Piedras, Puerto Rico
Immordino, Charles H.	225 W. 22nd St.	New York, N. Y.
Isaacs, John H.	1737 W. Howard St.	Chicago, Ill.
Iwig, Samuel C.	215 Estudillo Ave.	San Leandro, Calif.
Jacobson, Benjamin D.	187 Livingston Ave.	New Brunswick, N. J.
Jarvis, Harold F.	14110 Gratiot Ave.	Detroit, Mich.
Johnson, Carl E.	Mayo Clinic	Rochester, Minn.
Johnson, Vernal H.	2279 Jackson Ave.	Ogden, Utah
Johnstone, Robert E.	104 Wm. H. Taft Rd.	Cincinnati, Ohio
Jones, George R.	820 West Franklin	Richmond, Va.
Jones, Harry E.	108 Interstate Bldg.	Chattanooga, Tenn.
Jones, Paxton L.	3031 Market St.	Youngstown, Ohio
Juskowitz, Norman B.	1749 Grand Concourse	Bronx, New York
Kaiser, Irwin H.	University Hospitals	Minneapolis, Minn.
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Kamm, Michael L.	2560 Bancroft Way	Berkeley, Calif.
Kaplan, Henry M.	282 Wooster St.	New Britain, Conn.
Karam, James J.	1011 Cleveland Ave.	Canton, Ohio
Kassman, Noah J.	301 West State St.	Ithaca, N. Y.
Keller, Earl B., Jr.	517 Cooper St.	Camden, N. J.
Keller, Florence	158 Whitney Ave.	New Haven, Conn.
Kellogg, Pearson C.	2728 "J" St.	Sacramento, Calif.
Kennett, William	500 Arguello St.	Redwood City, Calif.
Kenney, James F.	203 Commonwealth	Boston, Mass.
Kieffer, John P.	39 Congress St.	Pasadena, Calif.
King, John A.	1521 Delachaise St.	New Orleans, La.
Klarich, Philip	323 S. 18th St.	Philadelphia, Pa.
Klinger, Siegfried	674 Madison Ave.	Albany, N. Y.
Kneer, William F.	28 Lowell Rd.	Kenmore, N. Y.
Kozlow, Louise A.	4274 N. Woodward	Royal Oak, Mich.
La Hood, Michael J.	17555 James Couzins	Detroit, Mich.
Lane, Francis R.	319 Longwood	Boston, Mass.
Langmade, Charles F.	127 N. Madison	Pasadena, Calif.
Lenahan, John P.	3890 Rocky River Dr.	Cleveland, Ohio
Lester, William M.	272 Boulevard N. E.	Atlanta, Ga.
Lewis, Lawrence C., Jr.	1121 Madison Ave.	Memphis, Tenn.
Liggett, Charles L.	1015 Polly	Baytown, Texas
Livingston, Elias	591 Stuyvesant	Irvington, N. J.
(Single certification in *Obstetrics* only)		
Lovett, Benjamin F., Jr.	618 Benson St.	Camden, N. J.
Lyons, Thomas J., Jr.	7 Dundee Ave.	Babylon, L. I., N. Y.
McCaw, William H.	114 S. Magdalen St.	San Angelo, Texas
McCune, Wallace H.	8208 Fenton St.	Silver Springs, Md.
McCune, William W.	1505 Elizabeth Ave.	Charlotte, N. C.
McHenry, Armand G., Jr.	Grand and Desiard Sts.	Monroe, La.
McKeogh, Robert P.	121 Lawrence St.	Gardner, Mass.
McLean, William F.	502 W. 13th St.	Austin, Texas
McVann, Robert M.	127 N. Madison Ave.	Pasadena, Calif.
Mackey, John E.	3209 N. Meridian St.	Indianapolis, Ind.
Madell, Warren	375 E. Main St.	Bay Shore, N. Y.
Manson, William W.	U.S. Naval Hospital	Portsmouth, Va.
Marcus, David	3805 31st Ave.	Long Island City, N. Y.
May, Harvey C.	18 Asylum St.	Hartford, Conn.
Marino, Frank S.	1061 Main St.	Danville, Va.
Marsella, John J.	310 Selling Bldg.	Portland, Ore.
Marshall, Alfred N.	1524 Elizabeth	Charlotte, N. C.
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Meloro, Patrick R.	712 N. 63rd St.	Philadelphia, Pa.
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Meyers, Sidney S.	19635 Mack Ave.	Grosse Pointe Woods, Mich.
Mickiewicz, M. Eugene	2935 Murdock Rd.	Wantagh, L. I., N. Y.
Miller, John S.	384 Post St.	San Francisco, Calif.
Miller, William S.	1233 Jefferson Bldg.	Peoria, Ill.
	(Single certification in *Obstetrics* only)	
Mize, William B.	215-217 W. Mulberry	Sherman, Texas
Mobley, Joseph C.	1055 Madison Ave.	Memphis, Tenn.
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Moore, Matthew B.	215 Branniff Bldg.	Tulsa, Okla.
Moore, Vernon B.	220 Textile Bldg.	Greenwood, S. C.
Moorhead, Jay O. C.	1052 Atlantic	Long Beach, Calif.
Moorhead, Joseph H.	U.S. Army Hospital (3420)	Fort Bragg, N. C.
Moorhead, Marie	1633 Medical Arts	Minneapolis, Minn.
Morrison, Robert H.	Naval Air Station, North Isl.	San Diego, Calif.
Movius, Earnest A.	2nd and Mission	Wenatchee, Wash.
Mundy, Carroll F.	2501 "G" St.	Bakersfield, Calif.
Nayfield, Ronald C.	990 S. Broad St.	Trenton, N. J.
	(Single certification in *Obstetrics* only)	
Neal, Jule C., Jr.	101 Professional Bldg.	Macon, Georgia
Nelson, Wallace W.	221 S. Fourth St.	Grand Forks, N. D.
Nenno, Donald J.	490 McKinley Pkwy.	Buffalo, N. Y.
Nettles, John B.	1819 W. Polk St.	Chicago, Ill.
Nicholson, Robert W.	U.S. Army Hospital	Fort Bragg, N. C.
Nicolay, Kenneth S.	Suite 106, 4635 Wyandotte	Kansas City, Mo.
Nix, Frank G.	1407 S. Carrollton	New Orleans, La.
Nix, Oscar G.	24 W. Chase	Pensacola, Fla.
Noyes, Robert W.	Stanford University Hospital	San Francisco, Calif.
O'Keeffe, Daniel F.	153 Bay St.	Glens Falls, N. Y.
Onorato, Robert R.	656 Yonkers Ave.	Yonkers, N. Y.
Osborne, William W.	631 Washington Ave.	Savannah, Ga.
Oser, Frank S., Jr.	921 Canal St.	New Orleans, La.
Otterholt, Erland R.	500 W. Milwaukee	Janesville, Wis.
Paquin, Jean E.	1835 Eye St., N.W.	Washington, D. C.
Parker, Roy T.	U.S. Naval Hospital	Camp LeJeune, N. C.
Parker, Samuel L., Jr.	Kinston Clinic	Kinston, N. C.
Parkinson, Edwin B.	Monument and Lombardy	Richmond, Va.
Payne, John W.	80 S. LaGrange Rd.	LaGrange, Ill.
Pennock, Thomas H.	1101 Delaware	Wilmington, Del.
Perlmutter, Irving K.	31-33 Lincoln Park	Newark, N. J.
Perry, John H., Jr.	5th and Broad Sts.	Wichita Falls, Texas
Pickhardt, Woodrow L.	Walter Reed Army Center	Washington, D. C.
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	(Single certification in *Obstetrics* only)	
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Powers, Harry T.	151 Rock St.	Fall River, Mass.
Poyas, Morton L.	916 W. State St.	Trenton, N. J.
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Ratzloff, Dan O.	614 Rose Bldg.	Cleveland, Ohio
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Reed, Theodore P.	527 Brookhurst Ave.	Narberth, Pa.
Reichman, Sidney C.	Maxwell Air Force Base	Montgomery, Ala.
Reisner, Lewis C.	408 Monongahela Bldg.	Morgantown, W. Va.
Reist, Vorris M.	U.S. Naval Hospital	Bainbridge, Md.
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Rice, Thomas J.	650 S. Central Ave.	Marshfield, Wis.
Richards, Lee W., Jr.	21 Western Ave.	Augusta, Mo.
Richardson, Augustus	710 Peachtree, N. E.	Atlanta, Ga.
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Romney, Seymour L.	221 Longwood Ave.	Boston, Mass.
Rorebeck, Curtis G.	606 South Blvd.	Tampa, Fla.
Rosenberg, Kurt	41-15 51st St.	Woodside, N. Y.
Rubin, Nathan W.	626 DeKalb St.	Norristown, Pa.
Rundles, Charles H.	106 S. Richman	Albuquerque, N. M.
Ruskin, Richard A.	1035 Park Ave.	New York, N. Y.
Russell, Thomas E., Jr.	3901 N. Charles St.	Baltimore, Md.
Rutherford, Morrison	119 N. A St.	Oxnard, Calif.
Rutzen, Arthur C.	771 Fisher Bldg.	Detroit, Mich.
Sadler, John M.	2514 Bethel Church Rd.	Pittsburgh, Pa.
St. Hill, Clyde E.	409 Stuyvesant Ave.	Brooklyn, N. Y.
Sargent, Carlton W.	U.S. Army Hospital	Fort Sill, Okla.
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Sharp, Merle C.	120 N. Lafayette Blvd.	South Bend, Ind.
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Shettles, Landrum B.	180 Fort Washington	New York, N. Y.
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Shreve, Robert W.	10 N. Main St.	W. Hartford, Conn.
Silvis, John S.	550 Grant St.	Pittsburgh, Pa.
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Smith, John H.	303 N. Main St.	Rockford, Ill.
Smith, Philip L.	2902 S. Fairfield	Fort Wayne, Ind.
Smith, Reginald A.	Mayo Clinic	Rochester, Minn.
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Taylor, Thomas U., II	650 Fifth Ave.	Fort Worth, Texas
Terry, Jules S.	2685 Main St.	Bridgeport, Conn.
Theurer, Henry A., Jr.	60 S. 4th East	Salt Lake City, Utah
Tomlinson, David R.	2144 Burdett Ave.	Troy, N. Y.
Traina, Salvatore R.	534 High St.	W. Medford, Mass.
Travis, Bane T.	1603 Central Ave.	Cheyenne, Wyo.
Trodella, George P.	168 Forst St.	Medford, Mass.
Troyan, Beatrice P.	255 S. 17th St.	Philadelphia, Pa.
Twombly, Gray H.	842 Park Ave.	New York, N. Y.
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Vanden Berg, William C.	Blodgett Hospital Medical Bldg.	Grand Rapids, Mich.
Verwys, A. L., Hubert	815 Alger St. S.E.	Grand Rapids, Mich.
Waddington, Arthur W. W.	2014 Delancey Pl.	Philadelphia, Pa.
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Waldrop, Grayson S.	214 Bryan Bldg.	Raleigh, N. C.
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Warder, Thomas F.	725 Bennie Dillon Bldg.	Nashville, Tenn.
Warren, John F.	6805 Baltimore Blvd.	College Park, Md.
Waters, Philip C.	307 S. 12th Ave.	Yakima, Wash.
Watson, Asa C., Jr.	815 Fifth Ave.	Fort Worth, Texas
Watts, Joseph	742 Maccabees Bldg.	Detroit, Mich.
Way, George T. C.	28 Garfield Pl.	Poughkeepsie, N. Y.
Weinfurtner, Bernard J.	U.S. Naval Station, Inf. N.N. 127, c/o P.M.	Seattle, Wash.
Wellborn, William R., Jr.	307 Ramsey St.	Bluefield, W. Va.
Wellenbach, Burton L.	269 S. 19th St.	Philadelphia, Pa.
Weller, Ralph N.	713 Genesee St.	Syracuse, N. Y.
Wheeler, Lillian G.	1915 16th St., N.W.	Washington, D. C.
Whitaker, Blenn A.	125 E. Glenoaks	Glendale, Calif.
Whittaker, Francis M., Jr.	70 N. 15th St.	San Jose, Calif.
Willson, Dean D.	92 E. Division St.	Fond du Lac, Wis.
Wilson, Arthur L.	8 S. Washington	Winchester, Va.
Wolf, Warren A.	803 Amity St.	Homestead, Pa.
Wood, Dwight R.	85 Jefferson St.	Hartford, Conn.
Woodard, Lawrence E.	3244 E. Douglas	Wichita, Kan.
Woodward, Clarence E.	34-40 S. Bedford Rd.	Mt. Kisco, N. Y.
Woolsey, Carl T.	710 Boston Bldg.	Salt Lake City, Utah
Wyatt, Robert H.	77 Bedford St.	Stamford, Conn.
Young, John J.	Madigan Army Hospital	Fort Lewis, Wash.
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Zibel, Milton	306 A North Eighth St.	Manitowoc, Wis.
Leavitt, Benjamin	857 North Main St.	Fall River, Mass.

(Single certification in *Obstetrics* only)

Canadian Society for the Study of Fertility

The first annual meeting of the Canadian Society for the Study of Fertility will be held in Montreal, Sept. 30 to Oct. 2, 1954. Inquiries should be addressed to

R. J. McDonald, M.D., Secretary
Woodstock, Ontario

Southern Society of Cancer Cytology

The Southern Society of Cancer Cytology will meet in St. Louis, Mo., Nov. 8 to 11. Inquiries should be addressed to the secretary,

J. Ernest Ayre, M.D.
1155 N. W. 14th St.
Miami, Fla.

Growth Hormone Symposium

An International Symposium on the Hypophyseal Growth Hormone, Its Nature and Actions, sponsored by the Henry Ford Hospital and the Edsel B. Ford Institute for Medical Research, will be held in the New Clinic Auditorium of the Henry Ford Hospital, Detroit, Oct. 27 to 29, 1954. Those interested should write to the

Program Committee
Henry Ford Hospital
Detroit 2, Mich.

Erratum

In the article, "The Relief of the Pains of Labor by the Continuous Intravenous Drip of Meperidine and Scopolamine," by Samuel S. Rosenfeld et al., in the May, 1954, issue of the Journal, in the sixth paragraph on page 1068, the amount of meperidine dissolved in 500 ml. of 5 per cent glucose in water should be 200 mg. or .2 Gm. instead of .002 Gm.